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BY
STEEN HANSEN

DISSERTATION SUBMITTED 2017

AALBORG UNIVERSITY
DENMARK

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Scientific work

Drone-Based Automatic External Defibrillators for Sudden Death? Do We Need More Courage or More Serenity?
Daniel B. Mark, Steen M. Hansen, Monique L. Starks, Mary L. Cummings
Circulation. 2017; 135:2466-2469

Electrocardiographic Preexcitation and Risk of Cardiovascular Morbidity and Mortality: Results From the Copenhagen ECG Study.
Skov MW, Rasmussen PV, Ghouse J, Hansen SM, Graff C, Olesen MS, Pietersen A, Torp-Pedersen C, Haunsø S, Køber L, Svendsen JH, Holst AG, Nielsen JB.
Circ Arrhythm Electrophysiol. 2017 Jun;10(6). pii: e004778. doi: 10.1161/CIRCEP.116.004778.

Accuracy of angina pectoris and acute coronary syndrome in the Danish National Patient Register.
Bork CS, Al-Zuhairi KS, Hansen SM, Delekta J, Joensen AM.
Dan Med J. 2017 May;64(5). pii: A5369.

Bystander Efforts and 1-Year Outcomes in Out-of-Hospital Cardiac Arrest.

Kragholm K, Wissenberg M, Mortensen RN, Hansen SM, Malta Hansen C, Thorsteinsson K, Rajan S, Lippert F, Folke F, Gislason G, Køber L, Fonager K, Jensen SE, Gerds TA, Torp-Pedersen C, Rasmussen BS.
N Engl J Med. 2017 May 4;376(18):1737-1747. doi: 10.1056/NEJMoa1601891.

Location of cardiac arrest and impact of pre-arrest chronic disease and medication use on survival.
Granfeldt A, Wissenberg M, Hansen SM, Lippert FK, Torp-Pedersen C, Christensen EF, Christiansen CF.
Resuscitation. 2017 May;114:113-120. doi: 10.1016/j.resuscitation.2017.02.026. Epub 2017 Mar 6.

Incidence and survival outcome according to heart rhythm during resuscitation attempt in out-of-hospital cardiac arrest patients with presumed cardiac etiology.
Rajan S, Folke F, Hansen SM, Hansen CM, Kragholm K, Gerds TA, Lippert FK, Karlsson L, Møller S, Køber L, Gislason GH, Torp-Pedersen C, Wissenberg M.
Resuscitation. 2017 May;114:157-163. doi: 10.1016/j.resuscitation.2016.12.021. Epub 2017 Jan 11.

Association between bystander cardiopulmonary resuscitation and redeemed prescriptions for antidepressants and anxiolytics in out-of-hospital cardiac arrest survivors.
Bundgaard K, Hansen SM, Mortensen RN, Wissenberg M, Hansen M, Lippert F, Gislason G, Køber L, Nielsen J, Torp-Pedersen C, Rasmussen BS, Kragholm K.
Resuscitation. 2017 Mar 29;115:32-38. doi: 10.1016/j.resuscitation.2017.03.032. [Epub ahead of print]

Bystander Defibrillation for Out-of-Hospital Cardiac Arrest in Public vs Residential Locations.
Hansen SM, Hansen CM, Folke F, Rajan S, Kragholm K, Ejlskov L, Gislason G, Køber L, Gerds TA, Hjortshøj S, Lippert F, Torp-Pedersen C, Wissenberg M.
JAMA Cardiol. 2017 Mar 15. doi: 10.1001/jamacardio.2017.0008. [Epub ahead of print]

Implantable cardioverter defibrillator and survival after out-of-hospital cardiac arrest due to acute myocardial infarction in Denmark in the years 2001-2012, a nationwide study.
Winther-Jensen M, Kjaergaard J, Lassen JF, Køber L, Torp-Pedersen C, Hansen SM, Lippert F, Kragholm K, Christensen EF, Hassager C.
Eur Heart J Acute Cardiovasc Care. 2017 Mar;6(2):144-154. doi: 10.1177/2048872616687115. Epub 2017 Jan 6.

Association of Bystander Cardiopulmonary Resuscitation and Survival According to Ambulance Response Times After Out-of-Hospital Cardiac Arrest.
Rajan S, Wissenberg M, Folke F, Hansen SM, Gerds TA, Kragholm K, Hansen CM, Karlsson L, Lippert FK, Køber L, Gislason GH, Torp-Pedersen C.
Circulation. 2016 Dec 20;134(25):2095-2104. Epub 2016 Nov 22.

Alcohol consumption and mortality in patients undergoing coronary artery bypass graft (CABG)-a register-based cohort study.
Grabas MP, Hansen SM, Torp-Pedersen C, Bøggild H, Ullits LR, Deding U, Nielsen BJ, Jensen PF, Overgaard C.
BMC Cardiovasc Disord. 2016 Nov 11;16(1):219.

Clinical predictors of shockable versus non-shockable rhythms in patients with out-of-hospital cardiac arrest.
Granfeldt A, Wissenberg M, Hansen SM, Lippert FK, Lang-Jensen T, Hendriksen OM, Torp-Pedersen C, Christensen EF, Christiansen CF.
Resuscitation. 2016 Nov;108:40-47. doi: 10.1016/j.resuscitation.2016.08.024. Epub 2016 Sep 8.

Prolonged cardiopulmonary resuscitation and outcomes after out-of-hospital cardiac arrest.
Rajan S, Folke F, Kragholm K, Hansen CM, Granger CB, Hansen SM, Peterson ED, Lippert FK, Søndergaard KB, Køber L, Gislason GH, Torp-Pedersen C, Wissenberg M.
Resuscitation. 2016 Aug;105:45-51. doi: 10.1016/j.resuscitation.2016.05.004. Epub 2016 May 17.

Temporal trends in survival after out-of-hospital cardiac arrest in patients with and without underlying chronic obstructive pulmonary disease.
Møller SG, Rajan S, Folke F, Hansen CM, Hansen SM, Kragholm K, Lippert FK, Karlsson L, Køber L, Torp-Pedersen C, Gislason GH, Wissenberg M.
Resuscitation. 2016 Jul;104:76-82

Prolonged cardiopulmonary resuscitation and outcomes after out-of-hospital cardiac arrest.
Rajan S, Folke F, Kragholm K, Hansen CM, Granger CB, Hansen SM, Peterson ED, Lippert FK, Søndergaard KB, Køber L, Gislason GH, Torp-Pedersen C, Wissenberg M.
Resuscitation. 2016 May 17;105:45-5

Home Care Providers to the Rescue: A Novel First responder Programme
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PLoS One. 2015 Oct 28;10(10):e0141352

Survival After Out-of-Hospital Cardiac Arrest in Relation to Age and Early Identification of Patients With Minimal Chance of Long-Term Survival
Mads Wissenberg · Fredrik Folke · Carolina Malta Hansen ·Freddy K Lippert · Kristian Kragholm · Bjarke Risgaard ·Shahzleen Rajan · Lena Karlsson · Kathrine Bach Søndergaard · Steen M Hansen · Rikke Normark Mortensen · Peter Weeke ·Erika Frischknecht Christensen · Søren L Nielsen · Gunnar H Gislason · Lars Køber · Christian Torp-Pedersen
Circulation. 2015 May 5;131(18):1536-45

Socioeconomic inequality and mortality - A regional Danish cohort study
Line R Ullits · Linda Ejlskov · Rikke N Mortensen · Steen M Hansen · Stella R J Kræmer · Henrik Vardinghus-Nielsen · Kirsten Fonager · Henrik Bøggild · Christian Torp-Pedersen · Charlotte Overgaard
BMC Public Health. 2015 May 14;15:490

Horse Riders Pernio
Steen Møller Hansen · Carsten Sauer Mikkelsen
Ugeskr Laeger. 2014 Jan 20;176(2)

Individual social capital and survival: A population study with 5-year follow-up
Linda Ejlskov · Rikke N Mortensen · Charlotte Overgaard · Line R B U Christensen · Henrik Vardinghus-Nielsen · Stella R J Kræmer· Mads Wissenberg · Steen M Hansen · Christian Torp-Pedersen ·Claus D Hansen
BMC Public Health. 2014 Oct 2;14:1025

Cell of origin associated classification of B-cell malignancies by gene signatures of the normal B-cell hierarchy.
Johnsen HE, Bergkvist KS, Schmitz A, Kjeldsen MK, Hansen SM, Gaihede M, Nørgaard MA, Bæch J, Grønholdt ML, Jensen FS, Johansen P, Bødker JS, Bøgsted M, Dybkær K; Myeloma Stem Cell Network (MSCNET).
Leuk Lymphoma. 2014 Jun;55(6):1251-60. doi: 10.3109/10428194.2013.839785. Epub 2013 Nov 1.

Paramandibular abscess following trans-oesophageal echocardiography
Steen M. Hansen, Søren S. Olesen, Gitte Nielsen, Jens Petersen
Eur Heart J Cardiovasc Imaging, 2012 jun;13(6):523. Doi: 10.1093/ehjci/jes007. Epub 2012 Feb 3.

The Cancer Stem Cell Concept in Multiple Myeloma - From Phenomenology to Characterisation.
Fogd K, Hansen SM, Madsen LH, Kjeldsen MK, Johnsen HE
European Haematology, vol. 4 p94-95, Touch Briefings, London.

ENGLISH SUMMARY

Early defibrillation of out-of-hospital cardiac arrest (OHCA) patients before the arrival of emergency medical services personnel has been associated with survival rates above 50%. Despite recent advancements in bystander resuscitative efforts (e.g. CPR rates), bystander defibrillation rates have remained low, and different strategic approaches to provide early defibrillation in different locations of arrest might be necessary.

By examining initiatives to facilitate bystander defibrillation in Denmark and two first responder programs, the overall goal of this PhD thesis was to identify opportunities and limitations for provision of early defibrillation in different locations of arrest. The main objectives were: 1) investigate if on-site AED dissemination and other nationwide initiatives to facilitate bystander defibrillation were associated with improved bystander defibrillation rates and survival in public and residential locations of arrest; 2) describe and evaluate a first responder program where home care providers functioned as first responders in the rural municipality of Frederikshavn, Denmark; and 3) investigate the association between the driving distance from the nearest fire station to an OHCA site and survival following first responder defibrillation in North Carolina, USA, where firefighters function as first responders.

As several initiatives were taken in Denmark to facilitate public access defibrillation, bystander defibrillation increased markedly from 1.2% in 2001 to 15.3% in 2012 in public locations of arrest. However, bystander defibrillation in residential locations of arrest remained unchanged during the study period (1.3% in 2001 to 1.3% in 2012). Thirty-day survival following bystander defibrillation increased from 8.3% in 2001/2002 to 57.5% in 2011/2012 in public locations; in residential locations, 30-day survival following bystander defibrillation increased from 0.0% in 2001/2002 to 25.6% in 2011/2012.

During the 1-year study period, the home care providers arrived before EMS personnel in 47% of OHCA cases. When the providers arrived before EMS, they performed CPR in 100% of cases, but an AED was only applied in 30% of cases and in only one case shock was delivered. In 93% of all home care provider dispatch calls the cardiac arrest was in a residential location. Unfortunately, a delay of 2 minutes and 23 seconds between the dispatch of EMS personnel and the home care providers was observed potentially constraining the benefit of the first responders. In total, 95% of the home care providers who had been dispatched to an OHCA event felt prepared in handling the OHCA situation as first responders.

Compared to EMS defibrillation, first responder defibrillation in the three study counties in North Carolina was associated within improved survival within 1 mile and 1-1.5 miles distances to the nearest fire station (Crude OR 2.01 [95%CI 1.46-2.78] and 1.61 [95%CI 1.10-2.35], respectively). At long distances (1.5-2 miles and >2 miles) survival did not differ between first responder defibrillation and EMS

defibrillation (Crude OR 0.77 [95%CI 0.48-1.21] and 0.97 [95%CI 0.67-1.41], respectively). No delay was observed between the dispatch of the first responders and EMS personnel in most cases.

Collectively, the findings in this thesis point to opportunities to improve bystander defibrillation rates in public locations of arrest by disseminating on-site registered AEDs linked to emergency medical dispatch centers and educating citizens in providing resuscitative efforts. However, the benefit of on-site AEDs in residential locations of arrest seems more limited. In residential and rural areas of arrest, first responders could be a solution to provide early defibrillation, but efforts to decrease dispatch delay and consider the location of and optimal travel distance of the first responder units should be prioritized.

DANISH SUMMARY/DANSK RESUMÉ

Ved tidlig defibrillering med en offentlig tilgængelig hjertestarter kan antallet af overlevere efter hjertestop uden for hospital være over 50%. I de seneste år er der sket væsentlige fremskridt i antallet af hjertestoppatienter, der modtager hjertelungeredning fra tilstedeværende hjertestopvidner, men antallet af patienter der stødes af en hjertestarter, er fortsat lav trods øget udbredelse af hjertestartere i det offentlige rum.

Formålet med denne afhandling var at undersøge muligheder samt barriere for at yde tidlig defibrillering i forskellige lokaliteter via tre studier: 1) at undersøge hvorvidt der er sket en stigning i antallet af hjertestoppatienter uden for hospital, der stødes af en hjertestarter i henholdsvis private og offentlige lokaliteter samt hvorvidt den efterfølgende overlevelse er forbedret i takt med, at der er taget initiativer for at øge tidlig defibrillering. De offentlige initiativer inkluderer blandt andre et register over offentlig tilgængelige hjertestartere, der er koblet til AMK-vagtcentralerne samt en øget uddannelse af den danske befolkning i at foretage genoplivning; 2) at beskrive og evaluere et program i Frederikshavn kommune, Danmark, hvor medarbejdere i hjemmeplejen blev udsendt parallelt med ambulancerne til hjertestoptilfælde uden for hospital (hjemmeplejen agerede som first responder til hjertestop uden for hospital); 3) undersøge hvorvidt afstanden til nærmeste brandstation har betydning for overlevelsen af hjertestoppatienter uden for hospital i North Carolina, USA, hvor brandmænd fungerer som first responder til akutte medicinske tilstande, herunder hjertestop.

I samme periode som adskillige initiativer blev taget for at øge tidlig defibrillering i Danmark, steg antallet af patienter stødt af en hjertestarter i offentlige områder fra 1,2% i 2001 til 15,3% i 2012. I private områder blev der ikke observeret nogen ændring (1,3% i 2001 til 1,3% i 2012). Tredive-dages overlevelsen efter tidlig defibrillering steg i offentlige områder fra 8,3% i 2001/2002 til 57,5% i 2011/2012. I private områder steg 30-dages overlevelsen fra 0,0% i 2001/2002 til 25,6% i 2011/2012.

I løbet af den etårige studieperiode ankom medarbejderen fra hjemmeplejen før ambulancepersonalet i 47% af hjertestoptilfældene. I situationer hvor hjemmplejen ankom før ambulancepersonalet, udførte hjemmeplejen i alle tilfælde hjertelungeredning, hvorimod en hjertestarter kun blev påsat i 30% af tilfældene resulterende i, at ét hjertestop blev defibrilleret. I 93% af alle hjemmeplejeudkald skete hjertestoppet i en privat lokalitet. Desværre blev der observeret en median latenstid på 2 minutter og 23 sekunder imellem udkald af ambulance og hjemmeplejen. I 95% af de tilfælde hvor en medarbejder fra hjemmeplejen havde været udsendt til et hjertestop, følte medarbejderen sig parat til at håndtere situationen.

Sammenlignet med defibrillering foretaget af ambulancepersonalet i North Carolina, USA, var overlevelsen ved defibrillering foretaget af en first responder højere

indenfor 1 mil samt 1-1,5 mil til nærmeste brandstation (henholdsvis OR 2.01 [95%CI 1.46-2.78] og 1.61 [95%CI 1.10-2.35]). Ved længere afstande til nærmeste brandstation (1,5-2 mil samt >2 mil) adskilte overlevelsen efter defibrillering ved en first responder sig ikke fra defibrillering foretaget af ambulancepersonalet (henholdsvis OR 0.77 [95%CI 0.48-1.21] og 0.97 [95%CI 0.67-1.41]). I de fleste tilfælde blev der ikke observeret nogen latenstid mellem udsendelse af first responders og konventionelt ambulancepersonale.

Samlet indikerer fundene i denne afhandling, at opsætning af registrerede hjertestartere tilkoblet AMK-vagtcentralerne sammen med andre initiativer kan øge antallet af patienter, der stødes før ambulancens ankomst i offentligt rum. Imidlertid kan andre initiativer være nødvendige i private områder. Her kan forskellige first responder programmer være gavnlige. Dog er det vigtigt at begrænse latenstiden før udsendelse af first responder, samt overveje lokaliteten og forventede kørselsafstande for first responders i forskellige områder for optimal effekt.

THIS PHD THESIS IS BASED ON THE FOLLOWING THREE PAPERS:

I. Bystander Defibrillation for Out-of-Hospital Cardiac Arrest in Public vs Residential Locations.

Hansen SM, Hansen CM, Folke F, Rajan S, Kragholm K, Ejlskov L, Gislason G, Køber L, Gerds TA, Hjortshøj S, Lippert F, Torp-Pedersen C, Wissenberg M.
JAMA Cardiol. 2017 Mar 15. [Epub ahead of print]
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II. Home Care Providers to the Rescue: A Novel First responder Programme

Steen M Hansen, Stig Brøndum, Grethe Thomas, Susanne R Rasmussen, Birgitte Kvist, Anette Christensen, Charlotte Lyng, Jan Lindberg, Torsten L B Lauritsen, Freddy K Lippert, Christian Torp-Pedersen, Poul A Hansen
PLoS One. 2015 Oct 28;10(10):e0141352
(*published*)

III. The association between driving distance from nearest fire station and survival of out-of-hospital cardiac arrest following early defibrillation by first responders

Steen M Hansen, Carolina Malta Hansen, Christopher B. Fordyce, Matthew Dupre, Lisa Monk, Clark Tyson, Christian Torp-Pedersen, Brian McNally, Kimberly Vellano, James Jollis, Christopher B. Granger, and the CARES Surveillance Group
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Since I started working as a researcher in 2014, my personal development and the learning curve I experienced have been incredible. I have met and collaborated with many dedicated and extremely bright people during this period without whom I would not have been able to complete this thesis and owe many thanks.

"If I have seen further it is by standing on the shoulders of Giants"
- Sir Isaac Newton, Letter to Robert Hook, 15 February 1676

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friendship. I miss our daily conversations at DCRI. Camilla and I hope to stay in touch regularly and hopefully see you soon in the future. Many thanks to Mayme, Dr. James Jollis, Clark and the rest of the cardiac arrest group for your help and guidance. Many thanks to all the incredible people at DCRI including Catherine, June, Seanna, Dixie, Tracy, Janelle and John. Many thanks to Maria Ratliff, Brian Frizelle, and Brandon Mitchell for your dedication and invaluable help with the first responder study.

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Steen Møller Hansen
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ABBREVIATIONS

AED	Automated external defibrillator
CARES	Cardiac Arrest Registry to Enchance Survival
CI	Confidence interval
CPR	Cardiopulmonary resuscitation
EMD	Emergency medical dispatch
EMS	Emergency medical services
EMT	Emergency medical technician
ICD-10	WHO International Classification of Diseases, 10th Edition
OHCA	Out-of-hospital cardiac arrest
OR	Odds ratio
Q1-Q3	1st and 3rd quartiles
ROSC	Return of spontaneous circulation

1 INTRODUCTION

A cardiac arrest is defined as cessation of cardiac mechanical activity with resultant absence of signs of circulation.[1] Traditionally, cardiac arrests have been divided as either an in-hospital or an out-of-hospital cardiac arrest (OHCA).[1,2] This thesis focuses on treatment of OHCA patients in the prehospital setting. Thus, for this thesis a cardiac arrest will refer to an OHCA.

Patients suffering an OHCA is a major health problem in both Europe and the United States with more than 275,000 and 420,000 OHCA cases per year, respectively.[3] In addition, survival following OHCA has been reported at about 10% in studies considering large study populations.[3,4]

1.1 EARLY DEFIBRILLATION AND AUTOMATED EXTERNAL DEFIBRILLATORS IN THE CHAIN OF SURVIVAL

To increase the chances of surviving an OHCA, prompt treatment of the OHCA patient initiated by bystanders and emergency medical services (EMS) personnel is vital.[5] The Chain of Survival summarizes four different links vital for a successful resuscitation of the OHCA patient; 1) Early recognition and call for help, 2) Early bystander cardiopulmonary resuscitation (CPR), 3) Early defibrillation, and 4) Early advanced life support and standardized post-resuscitation care.[5,6] Consequently, when CPR is initiated immediately after the OHCA occurs, survival can be doubled or quadrupled.[6–8] Further, the provision of early defibrillation (defibrillation before the arrival of EMS) within 3-5 min after arrest has been associated with high survival rates above 50% following OHCA.[9–12] However, if the time is too long before provision of early defibrillation after the onset of arrest, the chances of a successful defibrillation and subsequent increased survival quickly diminishes.[13–15] Thus, as defibrillation of OHCA patients is extremely time sensitive, different strategic approaches to provide early defibrillation in different locations of arrest as quickly as possible should be considered when organizing prehospital systems of OHCA care.

To facilitate early defibrillation, two overall strategies are available: on-site automated external defibrillators and first responders equipped with automated external defibrillators.

1.1.1 ON-SITE AUTOMATED EXTERNAL DEFIBRILLATORS

The first strategy involves placing on-site automated external defibrillators (AEDs) in communities where bystanders, in the event of an OHCA, can collect a nearby AED and provide bystander defibrillation within a short time after onset of arrest. Such public access defibrillation programs in communities can increase survival following OHCA[16], and bystander defibrillation using on-site AEDs have been associated with

OHCA survival rates as high as 74%.[11,16] Furthermore, it has been shown that layperson bystanders can operate on-site AEDs efficiently and safely in the event of an OHCA with minimum or no prior training.[17–19] Based on the high survival rates and recommendations from the American Heart Association and the European Resuscitation Council[19–21], publicly available AEDs have been disseminated widely in many countries to promote bystander defibrillation with hopes of increasing early defibrillation before the arrival of EMS personnel and ultimately improve OHCA survival rates.[22–24] While bystander CPR rates have improved in many countries in recent years following initiatives to increase bystander resuscitative efforts, bystander defibrillation has remained limited in broader populations despite a growing dissemination of public AEDs, and strategies to increase bystander defibrillation are warranted.[7,18,24–27] These limited rates of bystander defibrillation have been associated with different barriers to AED use. These barriers include: limited accessibility to AEDs placed in public locations; paradox placement of on-site AEDs in areas with a low incidence of OHCAs (such as office areas); and difficulties for OHCA bystanders with locating or remembering to locate and use a nearby on-site AED at the time of the OHCA.[16,28–34] In addition, on-site AEDs have a static placement by definition, which limits the coverage area of each AED as bystanders are to collect the AED and transport the AED to the cardiac arrest site which takes time.[29,35] Thus, in order to increase bystander defibrillation rates further, optimizing strategic placement, improving accessibility to nearby on-site AEDs, as well as enhancing the ability of bystanders to locate and use a nearby AED is essential. Another limitation to the overall efficacy of public access defibrillation programs relates to providing early defibrillation in residential locations.[18] Approximately 75% of all OHCAs occur in residential locations where conditions for early bystander defibrillation are less favorable compared to public arrests as fewer arrests are witnessed, patients generally are older and more chronically ill, fewer bystanders are available, and fewer patients receive bystander CPR. All such factors lower the chance of a shockable rhythm and limit the efficacy of AEDs.[7,16,18,33,36,37]

To increase bystander resuscitative efforts and facilitate bystander defibrillation in Denmark, several initiatives have been implemented. Apart from a general increase in disseminated AEDs, an AED network was established in 2007 and later linked on a nationwide scale to the emergency medical dispatch (EMD) centers. The information from the AED registry have since 2010 allowed the dispatcher at the EMD center to guide bystanders to a nearby accessible AED potentially addressing the problem with locating an AED.[38] In addition to guiding bystanders to the nearest accessible AED, dispatch-assisted CPR has been offered on a nationwide level since 2011, where EMD dispatch centers were staffed with healthcare professionals. Official recommendations from the Danish Health and Medicines Authority have been made regarding dissemination and accessibility of AEDs. Finally, every year since 2001 there has been a substantial increase in the number of Danish citizens who have received resuscitation training.[7] However, it remains unknown whether; 1) these combined initiatives have translated into higher bystander defibrillation rates, 2) if

potential improvements are consistent in public and residential locations of arrest, and ultimately 3) what is the survival rate of patients defibrillated by bystanders?

1.1.2 FIRST RESPONDERS EQUIPPED WITH AUTOMATED EXTERNAL DEFIBRILLATORS

The second strategy to provide early defibrillation involves mobile first responders equipped with AEDs who are dispatched in parallel with EMS personnel in the event of a medical emergency or OHCA. This solution offers an opportunity to extend the coverage area of an AED as the AED is transported to the cardiac arrest site by the dispatched first responder.[39] Further, first responders equipped with AEDs have the potential to provide early defibrillation in areas not easily covered by on-site AEDs, such as residential locations.[39] First responders who arrive at an OHCA site before EMS to initiate resuscitation have been associated with improvements in early defibrillation, performed CPR, and survival following OHCA.[39–42] Typically first responder programs have been conducted in urban and suburban areas.[43] However, reports from first responder programs conducted in rural districts have been encouraging, especially at reducing response times to the cardiac arrest site.[39,44] As such, first responder programs might help overcome the problems with providing early defibrillation in rural and residential locations.

Different first responder programs have been described, usually involving professionals or ordinary citizens in local communities such as firefighters, police officers, and/or layperson rescuers.[41,45–51] However, little is known about the factors that make first responder program successful or unsuccessful and in which locations they benefit the most.

In Denmark, home care providers usually perform the care of dependent elderly people. Most of the time the providers travel by car to visit citizens in their own homes. From October 1, 2012 to September 30, 2013 a first responder program was tested in a municipality of Denmark with mixed urban and rural settlements.[52] Following systematic basic life support training, including how to use an AED, these home care providers were dispatched in parallel with EMS to OHCA cases. This project is an example of a first responder program that includes professionals who are already present in local communities through their job when dispatched to OHCA emergencies.

In North Carolina, USA, firefighter first responders have been integrated in the emergency care system and are dispatched in parallel with the EMS in the event of a medical emergency, including OHCAs.[14,40] In most cases the firefighters are dispatched from their home fire station. Deployment of first responders in North Carolina have previously been shown to improve survival for OHCA patients by providing early defibrillation, when bystander CPR has already been initiated.[40]

1.2 AIMS OF THIS PHD THESIS

The overall aim of this PhD thesis is to identify opportunities for organizing prehospital care so that more OHCA patients can receive early defibrillation before ambulance arrival in different locations of arrest. By examining a Danish public access defibrillation solution and two different first responder programs, limitations to the different strategies will be identified too.

1. The aims of the first study (study I) were to investigate AED dissemination and other nationwide initiatives to facilitate bystander defibrillation to determine an association between initiatives and outcomes and to evaluate whether any change was consistent in public and residential locations of arrest.
2. The aims of the second study (Study II) were to describe and evaluate a Danish first responder program involving home care providers as first responders.
3. The aims of the third study (Study III) were to examine the association between the driving distance from the nearest fire station to an OHCA location and survival following first responder defibrillation in North Carolina, USA.

2 METHODS

2.1 STUDY I

2.1.1 SETTING AND POPULATION

This nationwide Danish cohort study included OHCAs from June 1, 2001, to December 31, 2012. Denmark covers about 42,900km^2 and has approximately 5.6 million inhabitants.[53]

2.1.2 DATA SOURCES AND STUDY POPULATION

For this study, we identified OHCAs from the Danish Cardiac Arrest Registry from June 1, 2001 through 2012. The data collection of OHCAs in the Danish Cardiac Arrest Registry was initiated in June 2001.[7] In Denmark, EMS personnel are dispatched to all suspected OHCAs and are subsequently required to complete a short case report based on the Utstein template[1] describing the OHCA incident. OHCA data are prospectively collected in the Danish Cardiac Arrest Registry, and only OHCA cases where resuscitative efforts are initiated by either EMS or bystanders are included in the registry. Thus, cases with obvious late signs of death where a resuscitative attempt was not initiated are not included in the registry.

For this study, the following OHCAs were excluded: 1) OHCAs with an invalid civil registration number; 2) second or third time OHCAs; 3) OHCA patients who arrived at a hospital with return of spontaneous circulation (ROSC) but did not have a related registered hospital admission; 4) OHCAs witnessed by EMS; 5) OHCAs with missing location of arrest and/or missing status on bystander defibrillation; and 6) OHCAs of presumed non-cardiac cause.

In Denmark, all citizens are assigned a unique civil registration number. This enables individual level linkage of information between nationwide registries. From the Danish National Population Registry, data regarding age, sex, and survival status were obtained. Admission dates, discharge dates, and discharge diagnoses from all hospitals were obtained from the Danish National Patient Registry. Causes of death were collected from the Danish Registry of Causes of Death. All discharge diagnoses and causes of death were defined according to the WHO International Classification of Diseases, 10th Edition (ICD-10).

Death certificates or discharge diagnosis codes were used to define the presumed cause of OHCA: cardiac disease, unknown disease or unexpected collapse were

defined as presumed cardiac cause. For OHCAs without the above-mentioned diagnoses diagnoses, but with other medical disorders were defined as non-cardiac causes. Causes such as trauma, drug-overdose, attempted suicide, or violent assault were also considered non-cardiac.[1]

2.1.3 INITIATIVES TO FACILITATE AED AVAILABILITY, AWARENESS AND USAGE

During the study period from 2001 to 2012, several initiatives were taken to strengthen bystander resuscitative efforts and facilitate AED usage. The initiatives include (selected initiatives are summarized in Figure 1):

1. The Danish AED Network:
    - The Danish AED network is a voluntary AED registry that includes information about the specific location of each AED, when the AED is available, who the person responsible for the AED is, and when maintenance of the AED is required. The network was established in 2007. Initially it was only available in Copenhagen. In 2010, the AED network became nationwide. In February 2010, the AED location information was linked with EMD centers in Copenhagen. The linkage became nationwide in 2011. Registration of AEDs bought by public funds in the network is mandatory.[38,54,55] The registration of privately owned AEDs in the network is voluntary, but highly recommended by AED vendors and the Danish Health and Medicines Authority. Since 2007, the specific location of each registered AED has been available to the public on a map located on the AED Network homepage.[55] In 2012, this map became further available by the use of a smartphone app. These maps allow all citizens to identify nearby AED locations in public and local environments.
2. Official recommendations:
    - In 2011, the Danish Health and Medicines Authority issued official recommendations concerning dissemination, strategic placement and accessibility of publicly available AEDs. In summary, the recommendations include that AEDs should be placed in high risk locations and the AED should be accessible 24 hours per day and seven days per week.[54]
3. Increased resuscitation training of the population:
    - During the study period, nationwide efforts were taken to strengthen and increase bystander resuscitation attempts. These include mandatory resuscitation training in elementary schools (2005) and when acquiring a driver's license (2006). Accordingly, there has been an increase in annually distributed first aid certificates from about 175,000 in 2001-2004 to about 300,000 in

2008-2011 and a concomitant increase in bystander cardiopulmonary resuscitation attempts from 21% in 2001 to 45% in 2010 was observed.[7]

4. Emergency medical dispatch centers:
    - Nationwide EMD centers have been staffed with health care professionals since 2011 who work as dispatchers. In addition, the dispatchers have adhered to a nationwide standard protocol. The protocol includes guidance of bystanders to perform CPR and collect a nearby registered AED in the event of a suspected OHCA.[38]
5. Disseminated AEDs
    - The accumulated amount of wholesale AEDs in Denmark was estimated at 3,000 AEDs in 2006 with an estimated increase to 15,000 AEDs in 2011.[54]

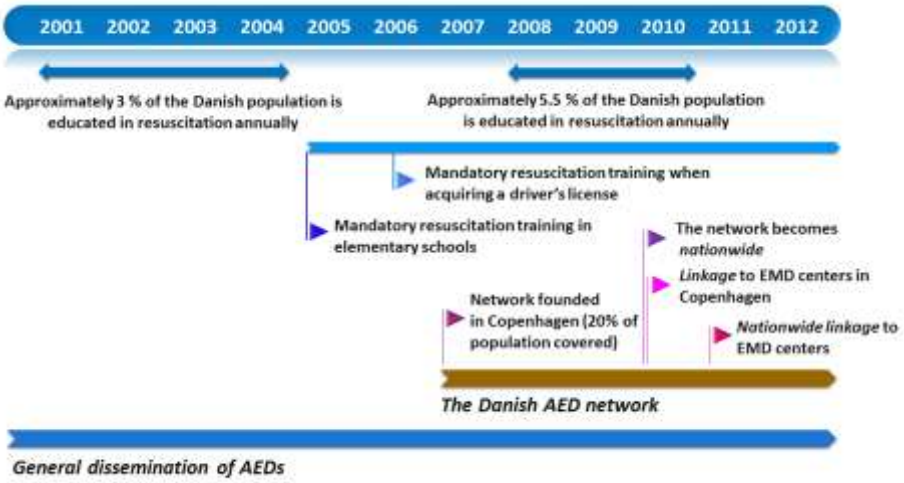

Figure 1: Selected initiatives to improve bystander resuscitative efforts from 2001 to 2012 in Denmark

2.1.4 LOCATION OF AUTOMATED EXTERNAL DEFIBRILLATORS

To determine the type of area covered by each AED we used the geocoded location of the AED (made available from the Danish AED network) and combined the AED location with area information (from publicly available municipal land-use plannings).[56] Land-use plannings in Denmark are continuously updated by mandatory municipal reportings and based on cadastral mappings of land parcels. "Cottage" - and "residential areas" (residential buildings cover more than 80% of the area) were

considered private areas. Areas with "mixed residential and businesses" (20%-80% of the area is mixed residential buildings and buildings used for business) were considered as mixed public/private. "Mixed public areas" (e.g. educational and healthcare buildings), "shopping areas", "business areas", "technical facilities" (e.g. power plants and water treatment plants), "recreational areas" (including sports facilities and parks), "rural areas" and "other areas" were all considered public locations. In the analysis of this study, the definition residential areas covered both residential and mixed residential and public areas.

2.1.5 STUDY OUTCOMES

The primary outcome was bystander defibrillation rate from 2001-2012 according to public and residential location of OHCA. Consequently, this only included patients where a shock was successfully delivered and not patients where AED pads were applied but no defibrillation was achieved. The secondary outcome was 30-day survival following OHCA according to public and residential locations of OHCA and bystander defibrillation status.

2.1.6 STATISTICS

Univariate logistic regression was used to analyze calendar trends in bystander defibrillation separately for public and residential locations of OHCA. For 30-day survival, we modelled the calendar trends, with or without bystander defibrillation separately for public and residential location of arrest, using logistic regression and restricted cubic splines (knots at years 2004, 2007 and 2011). To estimate the marginal effect of bystander defibrillation on 30-day survival following OHCA for each location, a multiple logistic regression model was constructed (adjusted for sex, age, calendar year, comorbidities available in Table 1, bystander CPR, and witnessed arrest). As in the previous models, calendar year was modelled utilizing restricted cubic splines with same knots as mentioned previously. Based on this regression model, the predicted mean 30-day survival was estimated (calculations were based on the g-formula[57,58]), separately for public and residential location of OHCA. The g-formula compares the outcomes that would have been observed if all patients had received one treatment or the other assuming that the covariates in the model account for differences other than treatment (exchangeability) and an overlap was present in the covariates between patients who received bystander defibrillation and those who did not receive bystander defibrillation (positivity). By this, the marginal gain related to the treatment was estimated. Bootstrap 95% confidence intervals (CI) were calculated.

A total of 5,424 patients with missing data on bystander defibrillation and/or location of arrest were excluded from the analyses. To analyze whether these patients with missing data were likely to introduce bias in our study, a comparison between results from the complete case analyses and results based on multiple imputation was made.[59]

First, missing data mechanisms and missing data pattern in our dataset were analyzed. Based on these analyses, no indication of informative missing data was identified, and the missing data mechanism was a mixture of missing completely at random and missing at random.[60,61] Second, the method of multivariate imputation by chained equations (MICE) was used.[59] Overall, 100 imputed datasets were constructed[62] using information from all covariates in Table in the appendix Paper I. The following variables were imputed in case of missing value: location of arrest, witnessed status, bystander CPR and bystander defibrillation, time interval, first recorded heart rhythm, and survival on arrival at the hospital. Finally, the mean bystander defibrillation probability estimated from the imputed datasets was compared with the complete case analysis results according to calendar year and location of arrest. This analysis is available in the appendix (see appendix Paper I, supplementary material).

Data management and data analysis were performed using SAS 9.4 (SAS Institute Inc.) and R, respectively.[63]

2.1.7 ETHICS

This study was approved by the Danish Data Protection Agency (2007-58-0015, internal reference GEH-2014-017/I-Suite nr. 02735). Ethical approval is not a requirement for retrospective registry-based studies in Denmark.

2.2 STUDY II

2.2.1 STUDY SETTING

This study was performed in the municipality of Frederikshavn in the North Denmark Region between October 1, 2012 and September 30, 2013.[52] Prior to the initiation date of the study, a run-in period from April 1, 2012 to September 30, 2012 was conducted to test for system errors and that satisfactory data collection was achieved.[64] During the study period, home care providers were equipped with AEDs and dispatched in parallel with conventional EMS personnel in the event of an OHCA. According to the study protocol, a home care provider should not be dispatched in the following cases; 1) the suspected OHCA patient was younger than 7 years, 2) the cause of the suspected OHCA was a trauma, a suicidal attempt or poisoning, 3) obvious signs of death described to the EMD dispatcher, 4) the OHCA was EMS witnessed, 5) the distance to the OHCA site from the location of the home care provider exceeded 10 km or 6) the OHCA site was in a neighbour municipality. When driving to the OHCA site, the home care providers were instructed to strictly adhere to official traffic regulations

e.g. applicable speed limits. The first home care provider who arrived at the OHCA site was instructed to focus on performing CPR. When or if a second home care provider arrived, an AED should be applied. To maintain the acquired skills during training, weekly test calls and monthly simulated dispatches were scheduled.[64]

The municipality of Frederikshavn is mainly rural, with scattered villages, farmed land and three urban centres. The three urban centres are Frederikshavn, Sæby and Skagen, with approximately 23,000, 9,000 and 8,500 inhabitants, respectively. The municipality covered 649 km^2 and had 61,119 inhabitants in 2012.[53]

Besides the home care providers being dispatched during the study period, a conventional two-tier system was activated when the EMD centre suspected an OHCA case. Emergency medical technicians (EMT) who could perform basic life support in defibrillator-equipped ambulances were dispatched together with paramedic staff in an emergency vehicle capable of delivering advanced life support. If available, a physician-staffed emergency vehicle was also dispatched.

Resuscitated OHCA patients were referred to the Aalborg University Hospital for advanced post-resuscitation care. The distance to this emergency hospital was within a range of 50-100 km.

During the study period, it was anticipated that home care providers would be dispatched to about 50% of 65-70 suspected OHCAs.

2.2.2 HOME CARE PROVIDERS AND RESUSCITATION TRAINING

The home care providers were employed by the municipality of Frederikshavn. Home care providers visit residents in need of care, usually frail and dependent elderly, to support the continued living of these residents in their own homes. The educational level of home care providers ranges from basic schooling to registered nurse training. According to the educational background of each provider, different tasks are performed from assistance with cleaning and personal hygiene to provision of medicine dispensations.

In total, 614 home care providers received a 2.5-hour training course in performing CPR and using an AED before being dispatched in the event of an OHCA. The course was based on European Resuscitation Council recommendations on resuscitation training at that time; each training involved 7-20 participants, and the course was planned by the Emergency Medical Services of North Denmark Region.[65]

2.2.3 THE HOME CARE PROVIDER EQUIPMENT AND DISPATCH TECHNOLOGY

A Zoll AED Plus system, including a kit containing scissors, gloves, pads, and cardiac-arrest action cards, was placed in each of 60 home care provider cars. Furthermore, the cars were equipped with a Samsung GSM Galaxy S Plus smartphone where a "SimaGo" application (SimaTech, Brondby, Denmark) was preinstalled. The SimaGo application allowed the EMD to GPS-track and activate a nearby home care provider in the event of a nearby OHCA. Upon activation of the dispatch system, the two nearest home care providers to the OHCA site were activated and received a text message call with information about the OHCA event and location. If the activated home care provider did not accept the call within 35 seconds, the call was automatically declined and the third nearest home care provider was activated. The home care providers were instructed to decline a call if they could not interrupt an ongoing task e.g. assisting a resident in taking a bath. During training, each home care provider received 30 min of instructions on how to handle the SimaGo dispatch application.

2.2.4 DATA COLLECTION

Similar to study I in this dissertation, EMS personnel dispatched to a suspected OHCA were required to complete a case file describing the event, including a narrative description of the OHCA event. The home care providers completed a case file for each dispatch, including descriptions of the tasks performed during the OHCA incident. In addition to the case file, the providers answered a questionnaire following activation and dispatch. For study II, data on self-evaluation of preparedness in handling the OHCA situation was evaluated. Preparedness was determined based on responses to a question on which extent the home care provider had felt prepared in the handling the OHCA situation. Four answers to this question were available; "largely, "to some extent", "to a lesser extent", and "to a small extent". Furthermore, electronic data such as SimaGo activation times and arrival times were collected in an OHCA case file together with the home care provider description. All these data were manually reviewed for study II to confirm the actual OHCA and validate whether the home care provider had arrived before EMS. Furthermore, details about patient status at hospital arrival were evaluated. Unfortunately, data on the home care provider arrival times proved unreliable in the first part of the study period because of either inaccurate manual registrations or errors in the GPS tracking. The GPS-related problems were corrected in a system update in mid-February 2013. Furthermore, the system was changed so the home care providers could not accidentally double push the button for manual time registration. Consequently, response times and distances from the activated home care provider to the OHCA site were only available after that time.

2.2.5 DATA ANALYSIS

We used Pearson's chi-squared test to test for differences between categorical variables. The Kruskal-Wallis rank sum test was used to test for differences in non-normally distributed continuous variables with more than two groups. A two-sided P-value<0.05 was considered statistically significant.

Data management and data analysis were performed using SAS 9.4 (SAS Institute Inc.) and R, respectively.[63]

2.2.6 ETHICS

The Danish Data Protection Agency (J.nr.: 2013-41-1844) approved this register-based study. The study required neither ethical approval by the local ethics committee nor written informed consent from patients.

2.3 STUDY III

2.3.1 STUDY DESIGN AND POPULATION

From the Cardiac Arrest Registry to Enhance Survival (CARES) registry[66], OHCAs from 2010 to 2014 from Durham, Mecklenburg and Wake counties in North Carolina, USA were included.[67] Each of the three counties has suburban and rural areas and a major city (Durham, Charlotte, and Raleigh, respectively). In 2014, the three study covered 22.6% of the population in North Carolina with a total population of 2,203,435 inhabitants.[68]

2.3.2 OUT-OF-HOSPITAL CARDIAC ARRESTS

The CARES registry contains information collected from the 911 emergency call centers, EMS agencies, and receiving hospitals for each cardiac arrest. The information includes demographic information (e.g. age, sex, ethnicity), resuscitation-specific information (e.g. bystander CPR, early defibrillation, first responder activities), arrest-specific information (e.g. location of arrest, witnessed or unwitnessed arrest, initial cardiac rhythm, and presumed etiology of arrest), and in-hospital data (e.g. survival until hospital discharge and Cerebral Performance Score at discharge).[66,69] Furthermore, the CARES dataset has precise geographic locations of 97% of the cardiac arrests.[40] Information on location of arrest was used to evaluate whether fire station locations were closer to cardiac arrests in public or residential locations on average.

2.3.3 EMS AND FIRST RESPONDERS IN NORTH CAROLINA, USA

When emergency medical dispatch centres are alerted about a suspected OHCA incidence in North Carolina, a two-tier system is activated where EMS personnel and first responders are dispatched simultaneously to the suspected OHCA site.

EMS personnel are defined as personnel who respond to medical emergencies as an official capacity (e.g. by responding to 911 calls) as part of an organized medical response team. Further, they are the official designated transport unit of the involved patient to a receiving hospital. The EMS ambulance response vehicles are usually distributed on the county road networks to ensure a low average response time (optimally within eight minutes) in all areas of the county.[70,71]

In comparison to EMS personnel, first responders are personnel who are dispatched to medical emergencies by emergency medical dispatch centers as an organized team in parallel with EMS. However, they are not the designated transporting unit of the involved patient to a receiving hospital.[40,72] In North Carolina, firefighters, police officers, rescue squads, and life-saving crew members function as first responders and are dispatched to the medical emergency site to initiate treatment before the arrival of EMS personnel.

The National Fire Protection Association's "Standard for Organization and Deployment of Fire Suppression Operations, Emergency Medical Operations, and Special Operations to the Public by Career Fire Departments" (NFPA 1710) states that non-volunteer fire departments should have a turnout time (time from alarm to the beginning of travel time) of maximum 80 seconds. Further, the NFPA 1710 states that the first fire engine company should have a travel time of less than four minutes. The same standard regarding travel time also applies for the firefighter first responder units equipped with AEDs.[73] Based on the NFPA 1710 requirements and ISO ratings fire stations are usually widespread in counties (ISO ratings are important for insurance premiums for residential and commercial properties – the better rating the lower premium).[74] During the study period, the firefighter first responders responded from a fire station in 96% of all dispatches in Durham County. This average included 94% of dispatches during daytime and 98% of dispatches during nighttime (data provided with courtesy of the Durham County Fire Department).

2.3.4 FIRE STATIONS

The location information for each fire station with firefighter first responders in Durham, Wake, and Mecklenburg were collected from online publicly available databases. Fire stations not operational during the study period were excluded. Only fire stations staffed with firefighters 24 hours per day and seven days per week were considered in this study, with a total of 147 fire stations.

2.3.5 SOCIOECONOMIC CHARACTERISTICS

For each cardiac arrest in the CARES dataset, North Carolina census tract information from the Census 2010 and the American Community Survey 2010-2014 were collected and added to the dataset. The collected data included the poverty rate, unemployment rates, and racial distributions to characterize the neighborhood tract for each OHCA. Areas were defined as: urban areas with ≥50,000; urban areas with 2,500 - 50,000; and rural areas with population clusters under 2,500 inhabitants.[67] Census tracts in the United States are small relatively permanent subdivisions of counties or equivalent entities. For the census tracts statistical information are collected decennially.[75] The American Community Survey is an ongoing survey by the United States Census Bureau. It gathers information more regularly than the decennial census.[76] For this study, American Community Survey tract level data were used.

2.3.6 OUTCOMES

The primary outcome measure was survival until hospital discharge. In Paper III in the Appendix, a secondary survival outcome with a favourable neurological outcome was defined as cerebral performance category 1 or 2 (good neurological function or moderate disability but independent in activities of daily living) at hospital discharge.[77,78]

2.3.7 GEOSPATIAL ANALYSIS

For all geospatial analyses, computer software ArcGis 10.4.1 was used including the geocoded location based on addresses.[79] Geocoded locations are available for approximately 97% of OHCAs in the CARES registry.[14,40] For each OHCA in the three study counties, the geocoded location was loaded in ArcGis together with the location of all fire stations. The driving distance in miles from the nearest fire station to each cardiac arrest was calculated using the Closest Facility feature in the ArcGis 10.4.1 Network Analyst extension.[80] As a road network for network analyses we used the Esri business analyst 2015 map data.[81] An example is provided in Figure 2 for Durham County using randomly generated points instead of actual locations of arrest cases.

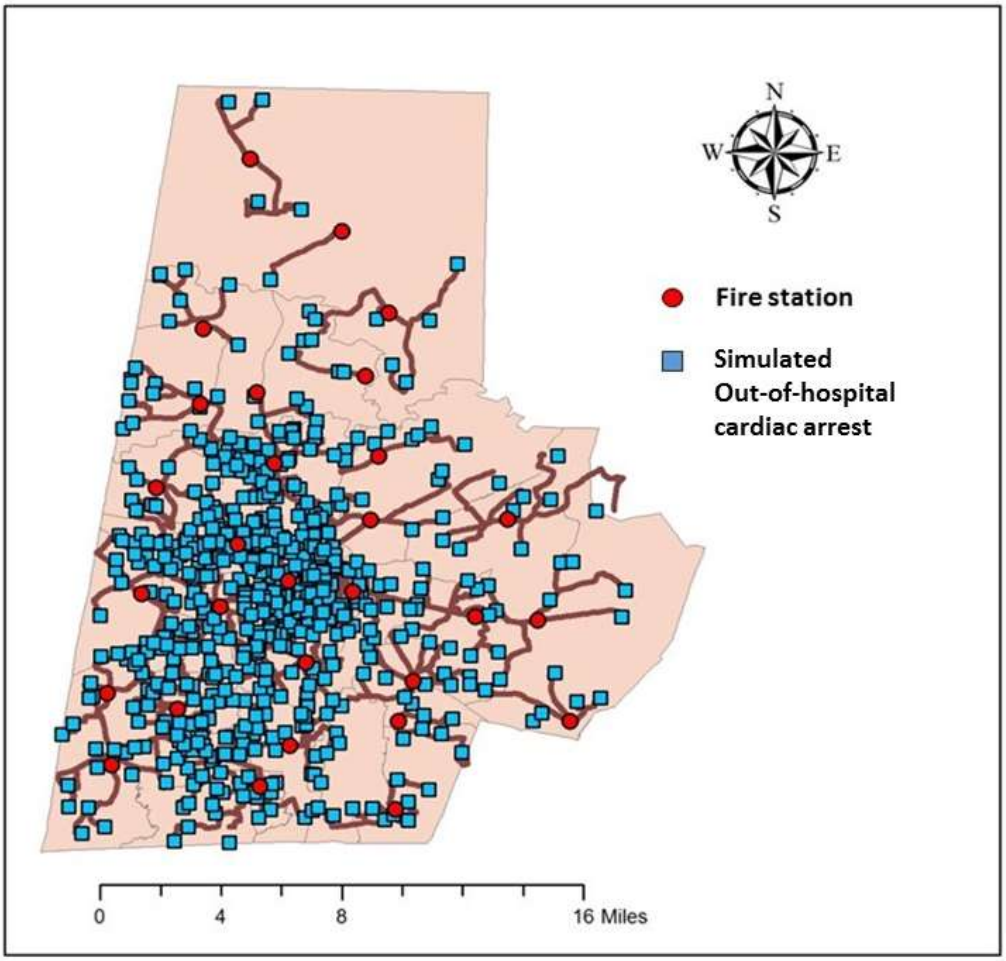

Figure 2: Fire stations in Durham County and calculated nearest driving distance routes from each fire station to randomly generated points (simulated out-of-hospital cardiac arrests).

2.3.8 STATISTICS

Categorical variables were presented as counts and percentages. Continuous variables were presented as medians with 1st and 3rd quartiles (Q1-Q3). For categorical variables, a chi square test was used to test for differences between the different categorical variables. For comparison of medians for more than two groups, the Kruskal-Wallis rank sum test was used.

The calculated driving distances between the nearest fire station and the OHCAs were divided in four groups with cut values at 1 mile, 1.5 miles and 2 miles. Using logistic regression, the associations between first responder defibrillation at the different driving distances and survival at hospital discharge were estimated. Both crude and adjusted analyses were conducted. The adjusted analysis included age, sex, layperson CPR, witnessed arrest status, location of arrest, year of arrest, and neighborhood characteristics (unemployment rate, percentage of people in poverty [82,83], and white or other race). With EMS defibrillation as reference, odds ratios were calculated and presented with 95% confidence intervals. To examine the association between driving distance from nearest fire station to the OHCA sites and survival at discharge, restricted cubic splines with knots at 1 mile, 1.5 miles, and 2 miles were used to model the survival in a logistic regression (for these analyses driving distance was included in the regression model as a continuous variable). These analyses were done for patients who had received first responder defibrillation and EMS defibrillation. Finally, overall survival until hospital discharge was estimated according to driving distance to nearest fire station for all OHCA patients. Trends in survival until discharge according to the different driving distances were tested using univariate logistic regression.

Data management was performed using SAS 9.4 (SAS Institute Inc.). Data analysis was performed using R.[63]

3 RESULTS

This results section summarizes the main results from the three studies. For each of the three studies, a short background is available followed by the results. More results, tables and figures for each study are available in Papers I-III provided in the appendix, including supplemental material if available.

3.1 STUDY I

Background:
In Denmark, several initiatives to facilitate bystander resuscitation efforts, including bystander defibrillation, have been undertaken. This study examined whether these initiatives translated into increased bystander defibrillation rates and improved OHCA survival for both public and residential locations of arrest.

Results:
Of a total of 18,688 OHCAs in Denmark during 2001-2012, 4,783 (25.6%) occurred in public locations and 13,905 (74.4%) in residential locations. In total, 360 (1.9%) patients were defibrillated by bystanders during the study period; 243 (243 of 4,783, 5.1%) in public locations and 117 (117 of 13,905, 0.8%) in residential locations. Overall, the patients who received bystander defibrillation were younger, more frequently male, had fewer comorbidities, had more often witnessed arrest, and received more often bystander CPR compared with patients not defibrillated by bystanders (Table in Appendix Paper I).
During the study period, bystander defibrillation rates in public locations increased markedly from 1.2% [95%CI 0.4%–3.5%] in 2001 to 15.3% [95%CI 12.4%–18.7%] in 2012 (P<0.001), while bystander defibrillation in residential locations remained limited and unchanged from 1.3% [95%CI 0.6%–2.6%] in 2001 to 1.3% [95%CI 0.8%–1.9%] in 2012 (P=0.17) (Figure 3). From 2007 to 2012 there was a large increase in registered AEDs from 141 units to 7,800 units, respectively. Most of the registered AEDs were placed in a public location.

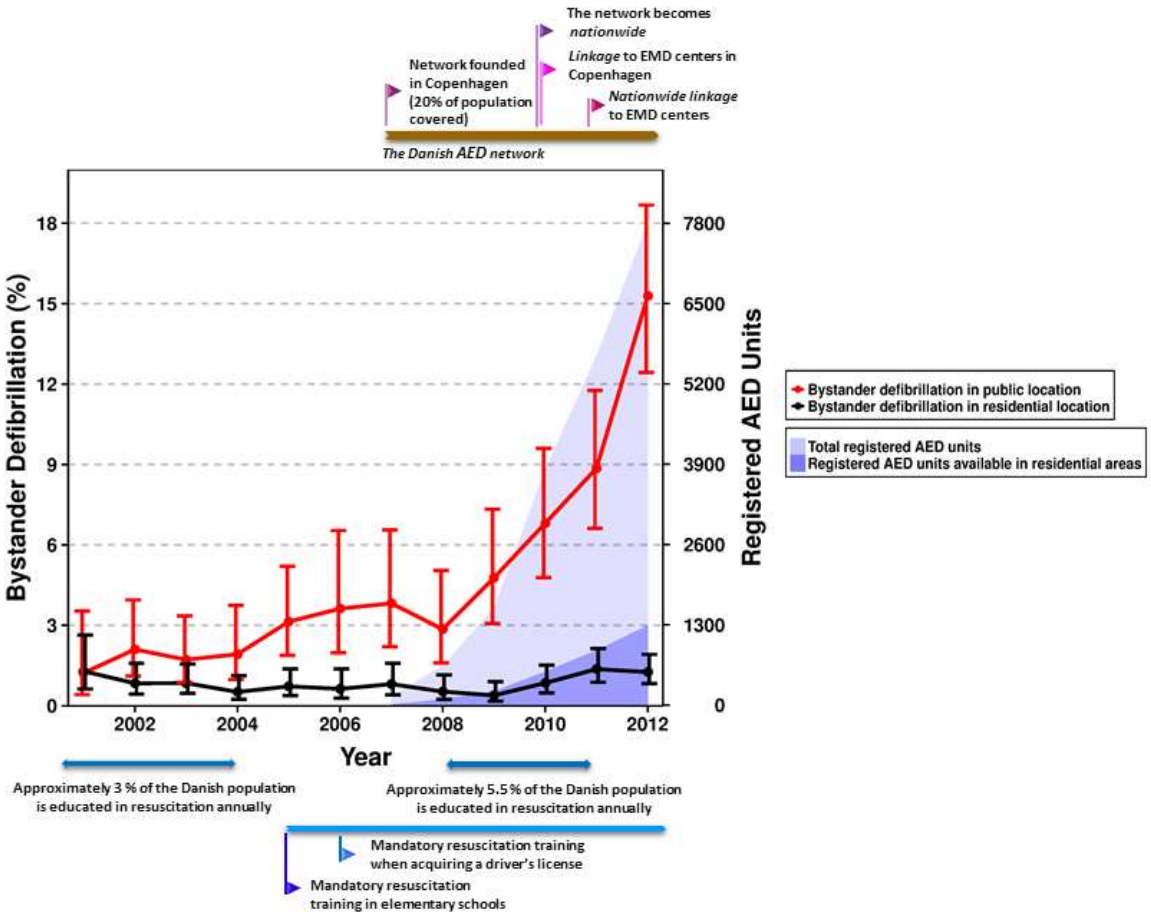

Figure 3: Bystander defibrillation according to the location of the out-of-hospital cardiac arrest and registered AED units in 2001 to 2012. Bystander defibrillation is shown together with number of registered AEDs over time and selected initiatives to increase bystander defibrillation. The figure includes the 95% confidence interval for each year. AED, automated external defibrillator; EMD, emergency medical dispatch

During the same study period, 30-day survival after being defibrillated by a bystander increased from 8.3% [95%CI 1.5%–35.4%] in 2001/2002 to 57.5% [95%CI 48.6%–66.0%] in 2011/2012 (P<0.001) in public locations. In residential locations, 30-day survival following bystander defibrillation increased from 0.0% [95%CI 0.0%–19.4%] in 2001/2002 to 25.6% [95%CI 14.6%–41.1%] in 2011/2012 (P<0.001). For

patients who were not defibrillated by bystanders, an increase in 30-day survival was also observed (Figure 4).

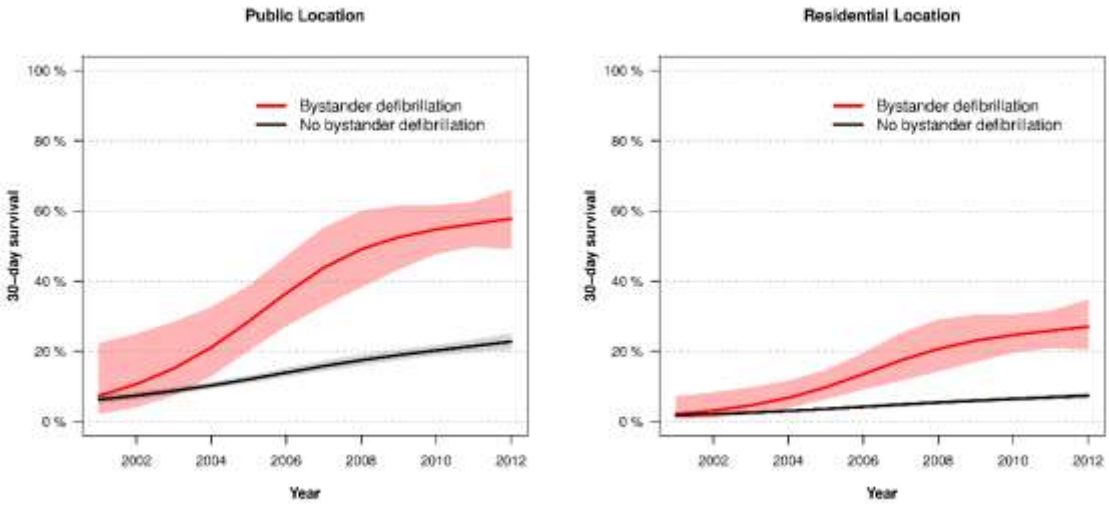

Figure 4: The 30-day survival according to the location of the out-of-hospital cardiac arrest and whether bystander defibrillation was performed. The results from logistic regression were not adjusted for patient characteristics, and restricted cubic splines were used to model calendar time trends.

3.1.1 ADJUSTED SURVIVAL ANALYSIS

Figure 5 illustrates the calculated average 30-day survival for the "all patients defibrillated by bystander" and "no patients defibrillated by bystander" scenarios and shows the marginal difference between the two scenarios separately for each location. In these adjusted analyses, bystander defibrillation was markedly associated with improved survival at the end of the study period in public locations. In residential locations, bystander defibrillation was also associated with improved survival at the end of the study period, but not as markedly.

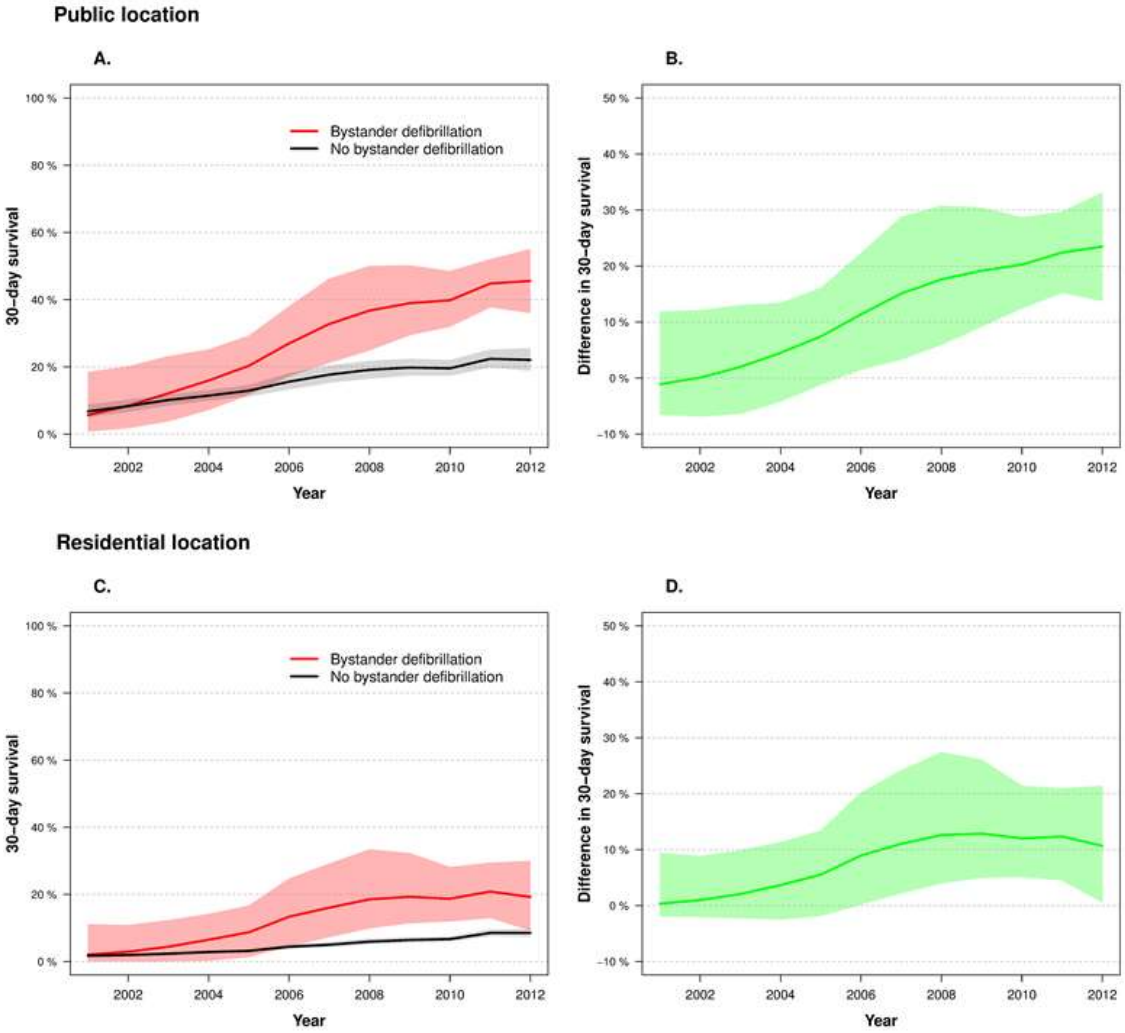

Figure 5: The adjusted 30-day survival according to the location of the out-of-hospital cardiac arrest and whether bystander defibrillation was performed. Panels A and C show the modelled average 30-day survival if every patient had been defibrillated (red lines) versus the projected average 30-day survival if no patient had been defibrillated (black lines). Projections were based on multiple logistic regression adjusted for sex, age, calendar year, comorbidities, bystander CPR, and witnessed arrest. Panels B and D show the differences in 30-day survival between the two scenarios for each location.

3.2 STUDY II

Background:
This study describes a Danish first responder program in a rural part of Denmark using home care providers, who were dispatched in parallel with conventional EMS personnel.

Results:
During the 1-year study period, 60 OHCAs occurred where a home care provider dispatch could have been considered. In 28 cases of the 60 cardiac arrests (46.7%) a home care provider first responder was successfully dispatched. In cases where a home care provider was successfully dispatched, a home care provider arrived before EMS in 35.7% of cases (10 of 28). In all 10 cases, a home care provider performed CPR. During three of the 10 arrests (30%) an AED analysis was achieved and one AED shock was delivered prior to EMS arrival. In 16 of the 28 successful dispatches (57.1%) the home care provider arrived after EMS personnel. EMS personnel and a home care provider arrived simultaneously on two of the 28 OHCA events. In 32 OHCA cases, a home care provider was not dispatched. In nine of the 32 cases (28.1%), a home care provider or other health care personnel was already present at the OHCA site and in two of the 32 cases (6.3%) the address was unknown. In 21 of the 32 cases (65.6%), a home care provider was not dispatched (Figure 6).

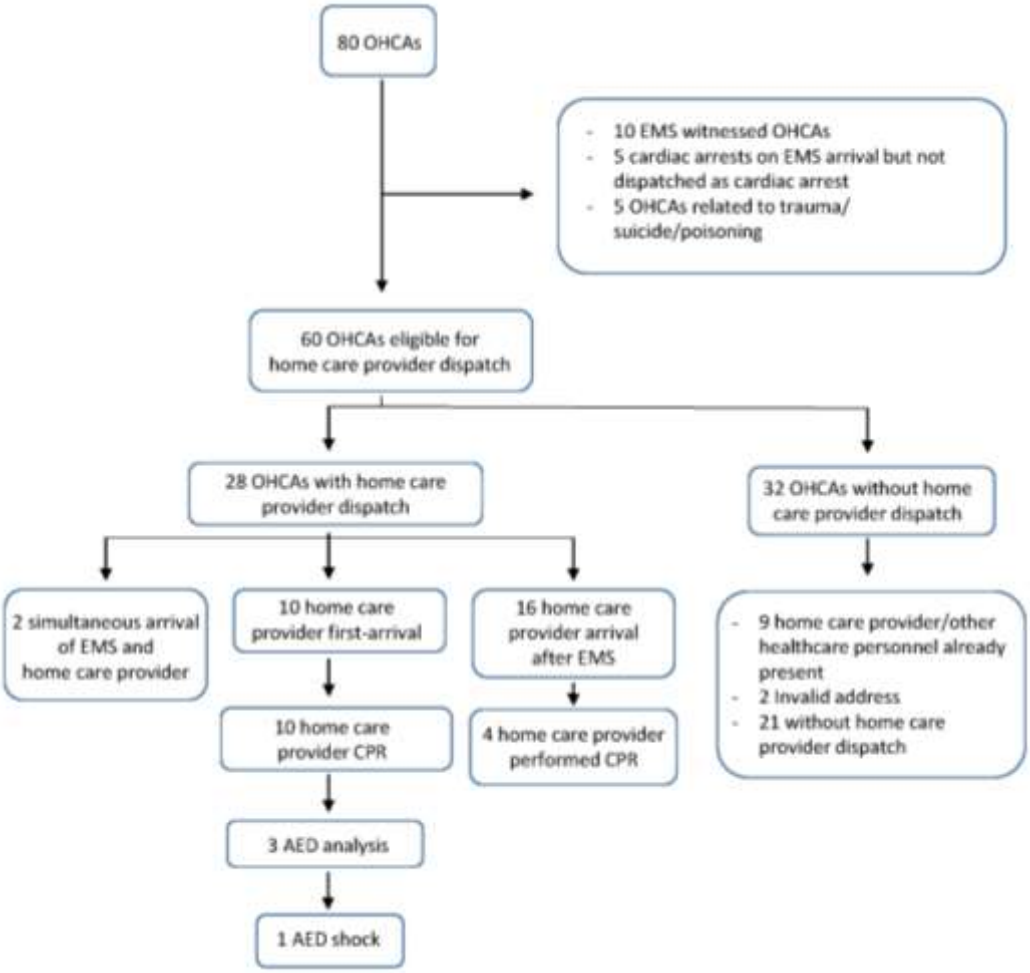

Figure 6: Study population in the home care provider first responder program.

Table 1: Out-of-hospital cardiac arrest characteristics where at least one home care provider was dispatched

	Dispatched					
	Home care provider first arrival n=10	**EMS first arrival** n=16	**Simultaneous arrival** n=2	**Total** n=28	**Missing data**	**P-value**
Age						
Median age in years {Q1-Q3}	77 {72, 80}	71 {64, 76}	70 {68, 73}	74 {68, 78}	1	0.28
Sex						
Men	6 (60)	12 (80)	1 (50)	19 (70)		
Women	4 (40)	3 (20)	1 (50)	8 (30)	1	0.45
Patient status at hospital arrival						
Dead	7 (70)	9 (60)	1 (50)	17 (63)		
Continued resuscitation attempt	1 (10)	1 (7)	1 (50)	3 (11)		
Achieved ROSC	2 (20)	5 (33)	0 (0)	7 (26)	1	0.39
EMS response time						
Median time (min:sec) {Q1-Q3 }	9:00 {6:00, 12:00}	5:00 {4:00, 9:00}	6:00 {4:00, 8:00}	07:00 {4:30, 10:00)		0.11
Home care provider response time*						
Median time (min:sec) {Q1-Q3 }	5:37 {5:25, 7:28}	11:03 {5:40, 12:26}	6:37 {5:02, 8:12}	7:41 {5:22, 11:27}	1	0.23
The distance of the nearest home care provider to OHCA site*						
Median distance (meters) {Q1-Q3 }	640 {591, 840}	988 {626, 2982}	1666,5 {389, 2944}	840 {389, 2785}		0.65

All results are n (%) unless otherwise specified. Q1-Q3 = 1st and 3rd quartiles EMS = Emergency medical service OHCA = Out-of-hospital cardiac arrest

* Only OHCA cases from mid-February 2013 until September 30 2013 (n = 21)

Table 1 summarizes OHCA characteristics where at least one home care provider was dispatched. The EMS response time trended to be shorter in cases where EMS arrived before the home care providers. Furthermore, the home care provider response times trended to be shorter in cases where they arrived before EMS compared with simultaneous or late arrivals.

In the study, 26 of the 28 (93%) home care provider dispatch calls with an actual cardiac arrest were in a residential location.

During the study period, 46 home care provider dispatch calls were executed from the emergency medical dispatch center. Two of the calls were unintentional as the cardiac arrest occurred in a neighbor municipal district. Four dispatch calls failed - one because of home care provider dispatch system malfunction, one because no home care provider was within 10 km of the cardiac arrest and two calls were not accepted by the home care providers. In 91 % (40/44) of the intentional dispatches, at least one home care provider successfully accepted the call and arrived at the suspected OHCA site. For 12 successful home care provider dispatches there were either no resuscitative efforts as either the OHCA patients had recognizable signs of death or in six cases the suspected OHCA incident was not a confirmed OHCA. For the 40 dispatches, there was a median delay between the dispatch of EMS personnel following the receipt of the emergency call to the dispatch of the home care providers of 2:23 min [Q1-Q3, 1:46, 3:38].

Following the home care provider dispatches, 42 questionnaires were answered by 47 home care providers who had been successfully dispatched to an OHCA situation. Fourty-one of 42 (98%) were sufficiently answered post-dispatch on what extent the home care provider felt prepared in handling the cardiac arrest situation. In total, 95% of the home care providers (39/41) felt “largely” or “to some extent” prepared at being dispatched to an OHCA incident and handle the situation as illustrated in figure 7.

Home care providers performed chest compressions in all ten first-arrivals. Home care providers performed pulmonary resuscitation in six arrest events prior to EMS arrival. In addition to three AED analyses, an AED was prepared in three cases where analysis was not achieved before EMS arrival. When the home care provider arrived after EMS, they assisted EMS in performing chest compressions during four events and pulmonary resuscitation in one event. In cases where a home care provider arrived first, after or together with EMS they took care of relatives 7, 8 and 1 times, respectively. In 4 of all 24 cases (16.7%), the home care providers had no functions during the cardiac arrest. In all of these cases the home care providers arrived late after EMS.

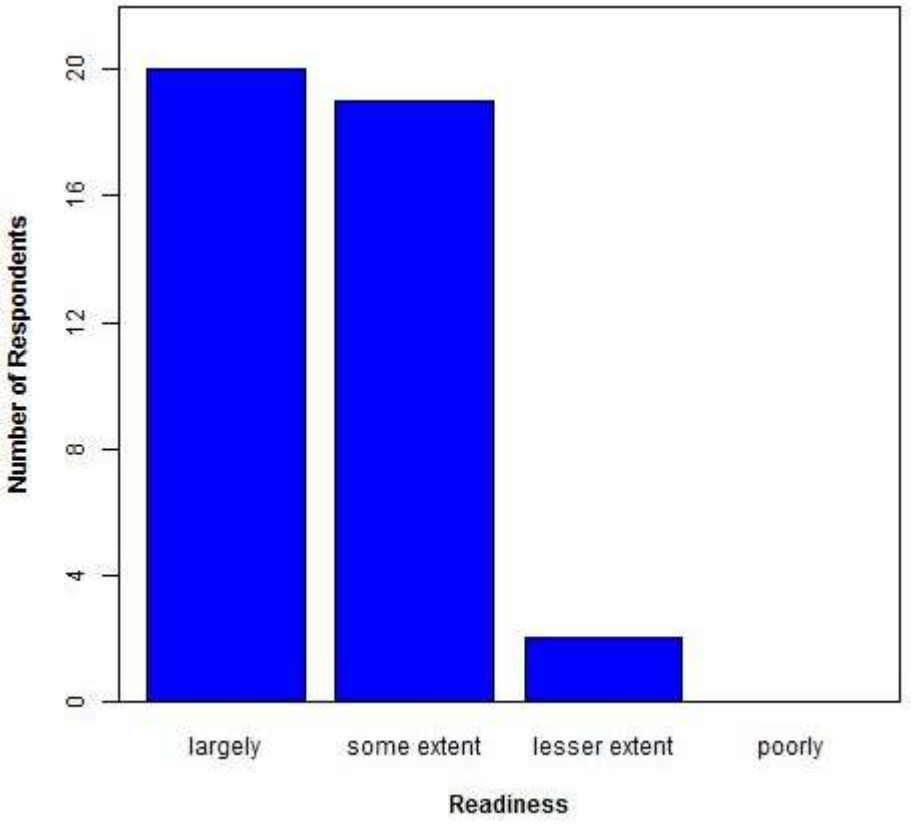

Figure 7: Home care provider readiness in handling the OHCA situation after an OHCA dispatch.

3.3 STUDY III

Background:
In North Carolina, USA, firefighter first responders are dispatched in the event of a medical emergency, including OHCA, in parallel with EMS personnel. In most cases the firefighters are dispatched from fire stations. In this study, the association between distance from nearest fire station to the cardiac arrest location and survival following first responder defibrillation was examined.

Results:
In total, 5,020 OHCAs were included as the study population. Most OHCA patients were male (61.4%). For OHCAs with the shortest distances (≤ 1 mile) from the nearest fire station, firefighter first responders more often applied an AED before EMS arrival

than at distances >2 miles (53.4% vs. 46.6%, respectively, P<0.001). At distances >2 miles, EMS personnel were more likely to apply the first AED (49.9% vs. 41.0% at distances <1 mile). CPR performed by laypersons before the arrival of first responders or EMS was more likely at distances >2miles (47.8%) than the shortest distances within 1 mile (41.8%) (P<0.001). Overall, laypersons initiated CPR in 45.9% of cases. For all patients defibrillated, firefighter first responders provided the defibrillation in 47.3% (776 of 1,642) of OHCA cases, EMS in 44.2% (725 of 1,642) of OHCA cases, and laypersons in 8.6% (141 of 1,642) of OHCA cases.

For distances from fire stations to OHCA sites within 1 mile, more OHCAs happened in a public location (31.7%) compared with distances > 2 miles (17.9%, P<0.001). For distances within 1 mile, the first responders arrived before EMS personnel in 71.2% of cases compared with 60.3% of cases at distances > 2 miles (P<0.001). Overall, most OHCAs occurred in urbanized areas (95.1%). Areas with short distance (≤1 mile) from fire stations to OHCA cases was an urbanized area in 97.1% of cases, and 89.6% of areas with a long distance (> 2 miles) (P<0.001) (Table 1 in Paper III in appendix).

We observed a trend in faster first responder response times within distances of 1 mile to fire stations compared with > 2 miles (5 min [Q1-Q3 4.0-6.8] vs. 7.6 min [Q1-Q3 6.2-9.3], P=0.006). Overall, there was a limited delay between the dispatch of the first responder compared with EMS personnel. During the study period, the firefighter first responders in Durham County responded from a fire station in 96% of all dispatches. This average included 94% of firefighter dispatches during daytime and 98% of dispatches during nighttime (data provided with courtesy of the Durham County Fire Department).

With EMS defibrillation as reference in crude logistic regression analyses, first responder defibrillation within 1 mile and 1-1.5 miles from nearest fire station was associated with an increased survival until hospital discharge following OHCA (OR 2.01 [95%CI 1.46-2.78] and OR 1.61 [95%CI 1.10-2.35], respectively). At 1.5-2.0 miles and >2.0 miles distance intervals, the survival following first responder defibrillation did not differ from survival following EMS defibrillation (OR 0.77 [95%CI 0.48-1.21] and OR 0.97 [95%CI 0.67-1.40, respectively) (figure 8). In adjusted logistic regression analysis, first responder defibrillation was associated with improved survival within 1 mile and 1-1.5 miles distance intervals (Figure 8).

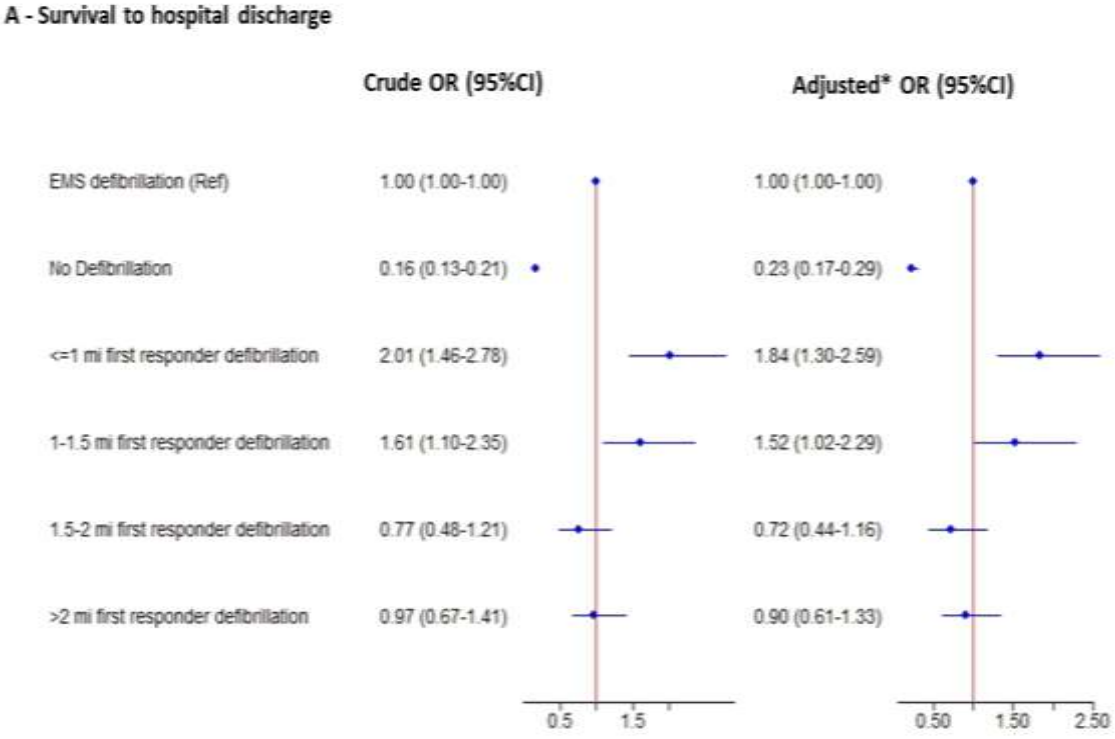

*Figure 8: Odds ratios of survival until discharge after out-of-hospital cardiac arrest (OHCA) for patients defibrillated by first responders at different driving distance intervals (1 mile, 1-1.5 miles, 1.5-2 miles, and above 2 miles) from nearest fire station to the OHCA site. * Adjusted for age, sex, location of arrest, witnessed arrest status, layperson CPR, year of arrest, and neighborhood characteristics (poverty rate, unemployment rate, and percentage of white or other race).*

Survival until hospital discharge after first responder defibrillation was significantly higher within the short distances compared with longer distances (P=0.001). For patients defibrillated by EMS, survival did not differ at the different driving distances from nearest fire station (P=0.58) (Figure 9).

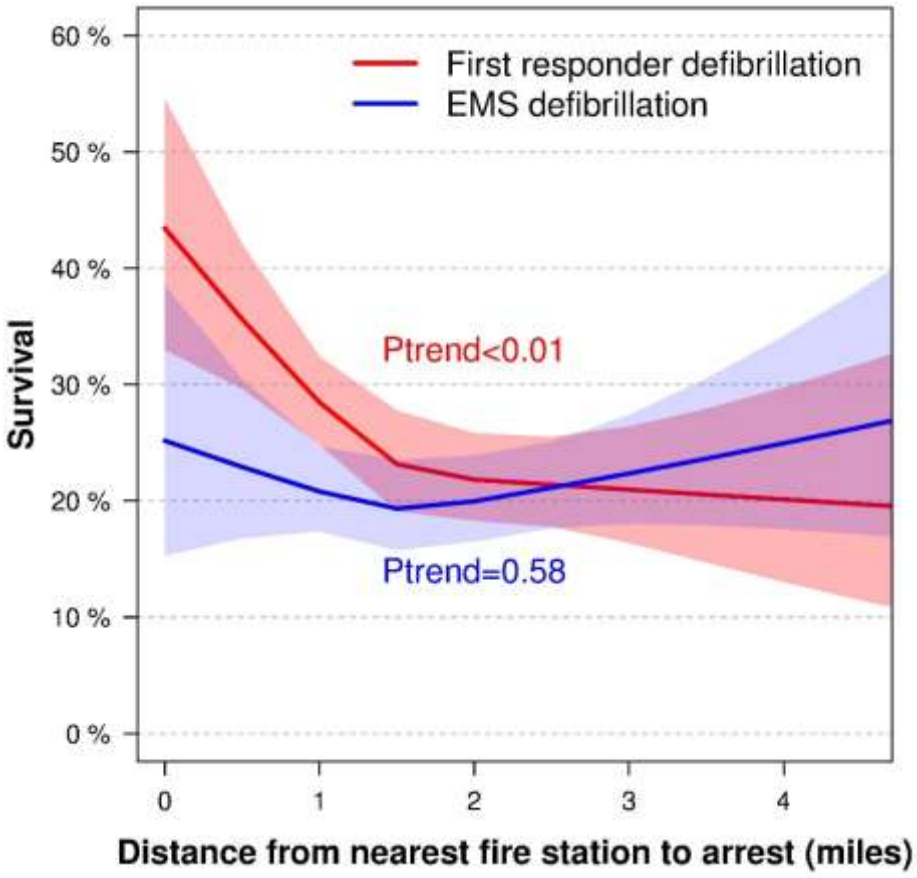

Figure 9: Survival following first responder or EMS defibrillation according to different driving distances from nearest fire station to the OHCA site.

Overall survival was higher at the shortest distances from fire stations compared with longer distances (P=0.04) (Figure 10).

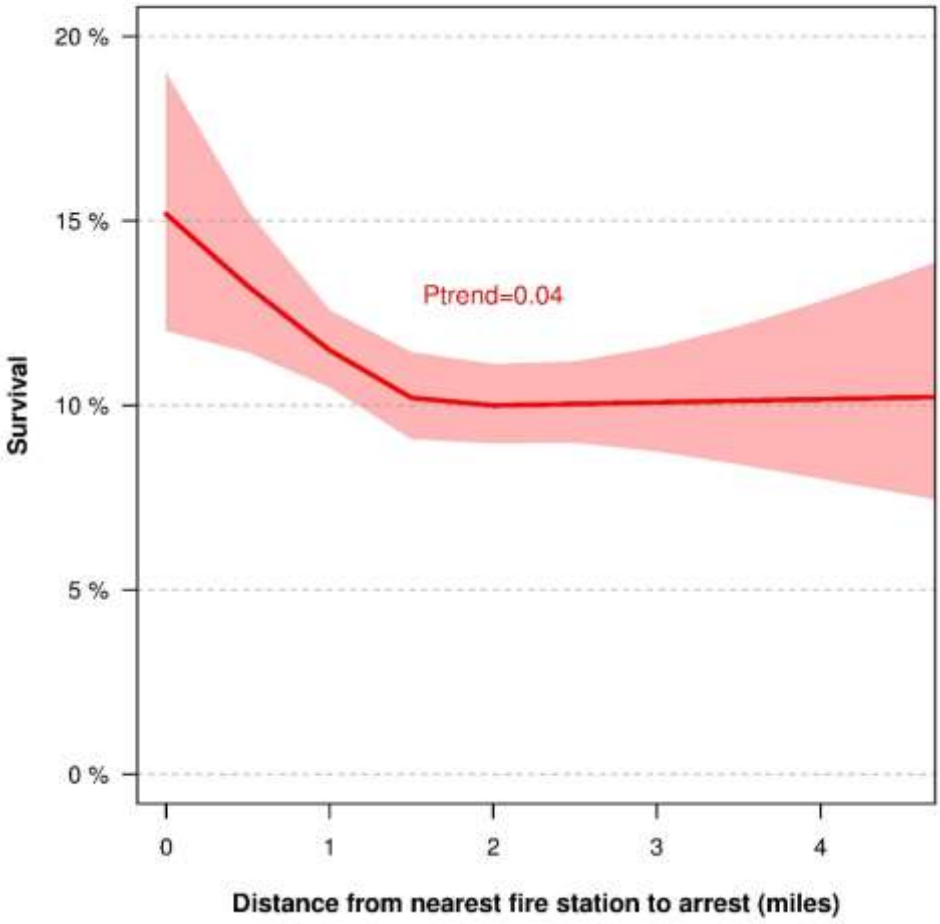

Figure 10: Overall out-of-hospital cardiac arrest survival at different driving distances to fire stations.

4 DISCUSSION

4.1 MAIN FINDINGS

The aims of this PhD thesis were to identify opportunities for providing early defibrillation of OHCA patients in different locations of arrest using different strategies. Furthermore, the aim was to identify potential limitations related to the different solutions described in this thesis.

Study I showed a remarkable increase in bystander defibrillation in public location from 1.2% in 2001 to 3.0% in 2008 and 15.3% in 2012. This increase occurred in the same period as several initiatives were taken to facilitate bystander resuscitative efforts, including bystander defibrillation. Importantly, the initiatives included more resuscitation training of the Danish population, general dissemination of AEDs, and the foundation of an AED registry making AED location available to dispatchers for dispatcher-assisted guidance to help bystanders locate a nearby AED. However, during the same period bystander defibrillation in residential locations remained limited at about 1%.

Study II described a first responder program where home care providers who work in local neighborhoods visiting frail elderly people in need of care were dispatched as first responders for OHCA emergencies. Overall, the study showed that home care providers felt confident in working as first responders following training in performing CPR and using an AED. In most cases the home care providers responded to OHCAs in residential locations offering an opportunity for providing early defibrillation in such locations. However, the providers arrived before the EMS in only 36% of provider dispatches to OHCA cases , and only one shock was delivered during the study period. A delay between the dispatch of EMS personnel and the home care providers at about 2 minutes and 20 seconds was observed.

Study III examined the survival outcomes following early defibrillation by first responders according to driving distances from fire stations to OHCA sites from where firefighter first responders responded in about 96% of dispatches. At distances shorter than approximately 1.5 miles, first responder defibrillation was associated with improved survival when compared with EMS defibrillation. No delay between the dispatch of EMS personnel and the first responders was observed. However, as more OHCAs happened in a public location in cases with short distance to fire stations compared with cases with longer distances this might constrain optimal provision of early defibrillation in residential locations.

4.2 DISSEMINATION OF AEDS AND BYSTANDER DEFIBRILLATION (STUDY I)

Previous studies have reported increases in bystander defibrillation rates over time, but the increases have not been as substantial as for bystander CPR rates.[7,8,23,31,41,84–86] Few studies have examined the association between the increases in bystander defibrillation rates and numbers of disseminated AED units, likely because of uncertainties regarding numbers and locations of disseminated AEDs. Recently, Kitamura et al published a study reporting an increase in bystander defibrillation from 1.1% in 2005 to 16.5% in 2013 as the cumulative numbers of public-access AEDs in Japan increased from 10,961 units in 2005 to 428,821 units in 2013.[23,84] The cumulative numbers of AEDs were estimated from AED wholesale data. However, only patients with a shockable rhythm and witnessed arrest of presumed cardiac cause were included in the study population. As some patients with a non-shockable rhythm might have had a shockable rhythm if an AED had been applied earlier[13,87], this constraint of the study population could distance the results from real life settings. Also, restricting the population to only bystander witnessed arrests seems problematic as patients with an unwitnessed arrest are clearly eligible for resuscitation attempts, including bystander defibrillation, despite a lower baseline chance of a positive outcome.[7,88] If patients without an EMS witnessed OHCA of presumed cardiac cause had been included in the study population by Kitamura et al., only about 0.8% of the study population received bystander defibrillation. Furthermore, the study did not provide new insights in which locations of arrest the public access AEDs provided most benefit as opposed to Study I in this thesis. Consequently, important details of potential value for decision makers when organizing prehospital systems of OHCA care might be overlooked. A study in urban Osaka, Japan, showed increasing bystander AED usage in public locations as AED units increased from 2005 to 2011.[31] No increase in patients defibrillated in residential locations was observed. This observation was speculated to be due to few available AEDs in residential areas. However, the study did not have information on AED dissemination in residential and public locations as in the present study. Additionally, the study was conducted in an urban environment and only bystander-witnessed arrests were considered as opposed to the nationwide Study I in this thesis considering both witnessed and unwitnessed OHCAs.

4.2.1 SURVIVAL FOLLOWING BYSTANDER DEFIBRILLATION

Placement and use of AEDs in public areas such as airports, sport facilities, offices, casinos and aircrafts have been associated with OHCA survival rates as high as 38%-56% and up to 74% for witnessed arrests defibrillated within three minutes.[9–12] At the end of the study period in Study I, the survival rate in a public non-selected national environment was 57.5% and comparable to the reported rates from the highly selected environments such as casinos and airports. In both public and residential locations of arrest, survival increased from low at the beginning of the study period to high at the

end. Concomitantly, patient survival for patients who did not receive bystander defibrillation also improved during the study period. A previous study by Wissenberg et al. described an increase in bystander CPR from 21.1% 2001 to 44.9% in 2010 and the increase was consistent in both sexes and different age groups.[7,89,90] Further, the increase in CPR bystander rates improved to above 60% in 2012.[91] These improvements in bystander resuscitative efforts[7,16,92,93] and other factors in the chain of survival, such as advanced post-resuscitation care[18,94], have previously been associated with an increase in survival following OHCA and are likely to explain some of the overall improved survival during the study period, also for patients who received bystander defibrillation.[7,18] Patients defibrillated by bystanders in both locations in Study I had characteristics favoring higher survival compared with patients not defibrillated (available in appendix Paper I) such as higher rates of performed bystander CPR, younger age, fewer diseases, and more witnessed arrests.[36] Accordingly, when considering such characteristics in our adjusted survival analysis, survival in public locations still improved during the study period but not as much as in the unadjusted analysis. Likewise, survival following bystander defibrillation in residential locations still improved at the end of the study period in the adjusted survival analysis, but less markedly than in public locations.

4.2.2 BYSTANDER DEFIBRILLATION ACCORDING TO LOCATION OF ARREST

Most OHCAs happen in residential locations (approximately 70%-85% of all OHCAs) [7,25,26], where chances for early defibrillation and survival are less favorable.[36] Study I showed that while a marked increase in bystander defibrillation was observed in public locations of OHCA, no increase was observed in residential locations despite 74% of all OHCAs occurring in residential locations. In study I, the OHCA patients in residential locations were older, had more diseases, fewer OHCAs were witnessed by bystanders, and bystander CPR rates were lower than in public locations. All these factors reduce the likelihood of a shockable heart rhythm and the chances of early defibrillation in residential locations.[37,88] Unfortunately Study I was unable to examine whether an AED had been applied but no shock was delivered as this data is not collected in the Danish Cardiac Arrest registry. However, Weisfeldt et al. reported that 41% of all bystander applied AEDs were in residential locations, but only 24% of all delivered shocks by bystanders happened in residential locations.[95] Further, another study by Weisfeldt et al. reported that chances of a shockable rhythm at first rhythm analysis were lower in residential locations compared with public locations when a first AED was applied by EMS or bystanders.[37] This supports that lack of a shockable heart rhythm was likely to have limited bystander defibrillation rates in residential locations in Study I. Only 17% of all the registered AEDs in Study I were placed near residential areas limiting the availability of AEDs in those cases. However, a study by Bardi et al. showed that placing AEDs in the homes of high-risk patients (patients with prior anterior wall myocardial infarction but not ICD candidates) did not improve survival for this group of patients.[33] Study I supports

previous observations that the effects of public access AEDs in residential locations seems limited, also when the location of a nearby AED is available at emergency medical dispatch centers allowing dispatcher-assisted guidance of bystanders to collect the AED. A rationale for this could be that in residential locations the number of bystanders at the OHCA site is limited compared with public locations and that the few bystanders should focus on providing CPR while waiting for help to arrive instead of searching for an AED.[18,96] In order to improve bystander defibrillation rates, studies have described strategies where first responders equipped with AEDs are dispatched in parallel with EMS to provide early defibrillation, including in residential areas.[39,86] Study I supports that new initiatives in residential areas, such as first responder programs with examples in Paper II and Paper III, should be considered to increase early defibrillation and thus allow a shock before an initial shockable heart rhythm deteriorates to a non-shockable rhythm.

4.3 EARLY DEFIBRILLATION PROVIDED BY FIRST RESPONDERS (PAPER II AND PAPER III)

Study II and Study III in this thesis described two first responder programs where home care providers and firefighters were dispatched in parallel with EMS for OHCA events, respectively.

In study II, all home care provider first responders were educated in performing basic life support and using an AED. In total, 95% of the home care providers who were dispatched to an OHCA and subsequently answered the questionnaire felt confident in handling the OHCA situation. This percentage was high and equal to or higher than satisfaction results from other first responder programs concerning fire-fighters, police officers, and lay-person volunteers[97–99]. This indicated that the training of the home care providers was valuable irrespective of home care provider educational background. Previous studies have reported that people trained in performing resuscitation are more likely to and confident at attempting resuscitation.[93,100,101] In North Carolina all firefighters are educated in providing basic treatment for medical emergencies.[102,103] This includes training in providing basic life support for OHCA cases, which is likely to decrease the time delay before an AED is applied and a shock is delivered.[17,104]

In Study II, the home care provider first responders were successfully dispatched to 28 cardiac arrests (47%). Further, they arrived before EMS in 10 of the 28 arrests (36%). A study by Zijlstra et al. from the Netherlands in a mixed urban-rural environment described a first responder program where layperson rescuers were dispatched to perform CPR or bring an AED to the OHCA site. The layperson first responders were dispatched in parallel with EMS and police officer first responders and activated in 58.1 % of all cardiac arrests.[39] In a first responder program from Stockholm, Sweden, laypersons were dispatched using a mobile phone setup. They arrived prior to EMS in 56% of all true OHCAs.[105] In an urban first responder study

from Sweden, fire-fighters were dispatched in 66% of all OHCAs and arrived before EMS in 36% of all dispatches.[46] An American metropolitan study reported that police officers equipped with AEDs arrived before EMS in 56% of cardiac arrests.[106] However, other American studies did not report the same high rate of police officer first-arrivals.[48,107] A study by Moore et al. described police volunteers and laypersons as first responders being dispatched to 40 % of all OHCA events and arrived before EMS in 47 % of cases in rural areas.[44] In Study III, the first responders arrived before EMS in 71% of OHCA cases at the shortest distances (≤1 mi) from nearest fire station to the OHCA site. At the longest distances (>2 mi), the rate of first responder arrivals before EMS was still high at 60% of OHCA cases. In addition, for both Study II and Study III, shorter first responder response times were observed for cases where the home care providers arrived before EMS and at the shortest distances from fire stations, respectively.

First responders are capable of providing both early defibrillation and CPR when arriving at the OHCA site and can improve CPR rates.[41,42] In study II, an AED was applied by a home care provider in 30% of first arrivals and one shock was delivered. In all ten home care provider first arrivals, CPR was provided. The first home care provider to arrive was instructed to focus on performing CPR. When or if an additional home care provider arrived, that person should prioritize the application of an AED. If primary use of AEDs had been prioritized, the number of AED analyses would probably have been higher. Optimally, efforts should be taken to improve rates of CPR performed by bystanders already present at the OHCA site[7] instead of organizing for a first responder to arrive and provide CPR, as delays in first initiated CPR and application of an AED are likely to decrease chances of early defibrillation and survival.[96,108]

4.3.1 FIRST RESPONDER DISPATCHES

For many different first responder programs, the first responders are only dispatched in parallel with EMS for OHCA events and not to other medical emergencies.[39,41,46,48,86] Likewise, the home care providers in Study II were only dispatched to suspected OHCA events. When the dispatcher receives the emergency call at the emergency medical dispatch center, identifying the medical emergency as an OHCA instead of e.g. a seizure or an unconscious patient from other causes can be time-consuming and the OHCA incident may remain unrecognized.[46,109,110] EMS personnel are immediately dispatched to the medical emergency despite the incident has not yet been recognized as an OHCA. Conversely, the OHCA has to be identified as an OHCA before the first responders, who are restricted to OHCA cases only, are dispatched. Consequently, a delay between the early dispatch EMS personnel and the dispatch of the first responders is likely to occur as illustrated in Study II and previous studies.[46,48] Such delays potentially limit the benefit of first responders, and can be hard to improve without increasing the chance of dispatching the first responders to non-cardiac arrest situations as illustrated in the study by Høyer et al.[51] In that study,

firefighter first responders were dispatched to suspected OHCAs in an urban environment. However, the definition of a suspected OHCA was widened to also include unconscious and unspecified emergency cases. The first responders arrived before EMS in 73% of all dispatches despite being in an urban environment where EMS response times were generally low. However, only in 4.9% of all dispatches the medical emergency dispatch was an actual OHCA.[51] In Langeland, a rural region of Denmark, a local first responder program has been established involving volunteer laypersons who are dispatched for many medical emergencies in parallel with EMS personnel. As in the study by Høyer et al., a high rate (94%) of first responder first arrivals was reported. However, the first responder dispatches were mostly other emergencies than OHCAs as only 4.5% of all dispatches were a suspected OHCA.[111] In North Carolina, USA, the firefighter first responders are dispatched to medical emergencies in parallel with EMS personnel and not only suspected OHCAs to treat the patient before the arrival of EMS personnel. This is likely to be an important reason, why the dispatch delay between EMS personnel and the first responders in Study III was limited. Furthermore, the firefighter first responders in Study III have the option to drive by siren to the OHCA site, potentially bypassing traffic. An option not available to e.g. layperson first responders or the home care providers in Study II.

4.3.2 OHCA FIRST RESPONDERS IN DIFFERENT LOCATIONS

In rural districts with lower population densities, EMS response times are likely to be longer compared with response times in areas with higher population densities.[112,113] This provides a rationale for using first responders in rural districts.[44,111] In study II, when the home care providers arrived before EMS, the median EMS response times were longer compared with EMS first arrivals or simultaneous arrivals. In study III, most OHCAs happened in urbanized areas. Most of the first responder first arrivals were at the shortest distances from fire stations where EMS response times tended to be lower than at longest distances from fire stations to the OHCA site.

Most cardiac arrests occur in residential locations where survival rates following arrest are lowest.[36] Many first responder programs have reported that the first responders were more likely to arrive before EMS in residential locations compared with other locations.[39,114] This was observed in Study II. In study III, the OHCAs being closer to fire stations were more likely in a public location than at longer distances. Thus, the geographic location of the fire stations favored OHCAs in public locations. This could potentially limit the benefit of early defibrillation provision in residential locations by these first responders.

4.3.3 FIRST RESPONDER COVERAGE DISTANCES

When implementing first responders in prehospital systems of OHCA care, the maximum distance between the OHCA site and the first responder location before the first responder is dispatched should be considered. Indeed, different maximum ranges

have been reported within the range of 500 m to 10 km in Study II.[42] In study III, survival after first responder defibrillation was higher within approximately 1-1.5 miles from the nearest fire station when compared with EMS defibrillation. When evaluating the importance of these driving distances, factors that could influence the observed association between the different driving distance ranges and survival following first responder defibrillation should be considered. These include any delays (e.g. dispatch delays, traffic, the skill level and experience of the first responders, and the ability to drive by siren) in the arrival of first responders, as such delays are likely to constrain the maximum distance that can be travelled by the first responder. Further, the maximum distance measures in previous studies have been straight-line (Euclidean) distances.[39,42] Such distances are shorter than actual distance travelled which could constrain the expected benefit of the first responders. In a previous layperson first responder program, some of the dispatched laypersons were to collect an on-site AED and bring it to the cardiac arrest site.[39] This increases the total travel distance and potentially limits the efficacy of the early defibrillation provided by such first responders. The home care providers in Study II were dispatched to OHCAs within a distance of 10km. However, when the home care providers arrived before EMS personnel the median distance travelled was 640m compared with approximately 1km and 1.5km for late and simultaneous arrivals, respectively. Consequently, the 10km maximum distance seems optimistic. However, restricting to shorter distances could result in low first responder coverage, especially in rural areas. In study II, EMS personnel were more likely to defibrillate the OHCA patient at the longest distances from nearest fire station compared with the shortest distances. However, first responders were still the first to defibrillate OHCA patient in almost half of cases at the longest distances where survival following first responder defibrillation was comparable to survival following EMS defibrillation. Consequently, the first responders can still help provide early defibrillation and improve overall survival at longer driving distances, including areas with long average EMS response times. However, lower survival rates following first responder defibrillation should be expected in such areas.

5 LIMITATIONS

5.1 STUDY I

Because of the observational design, Study I could not examine the impact of each initiative on the increase in bystander defibrillation rates over time. Furthermore, the design of the study cannot determine that the higher survival rates observed for patients defibrillated by bystanders was solely due to the increased early AED use. However, the results from our adjusted survival analysis did overall not differ significantly from our crude analyses in interpretation. However, unmeasured factors that are important for patient survival might be present in our study, such as higher quality CPR and more aggressive post-cardiac arrest care for patients who received bystander defibrillation. Further, data were not available on whether a registered AED was applied, but no defibrillation was achieved. Finally, data regarding whether a bystander was guided by a dispatcher to perform CPR and/or collect an AED were not available.[115]

Patients with missing data on bystander defibrillation and/or the location of the OHCA were excluded from the study population. To test whether it was likely that these missing data could introduce bias, we performed a sensitivity imputation analysis that included these excluded patients. The results from that analysis did not change our conclusions regarding the increase in bystander defibrillation in both locations over time (Paper I supplemental material in the Appendix).

Only data from AEDs registered in the Danish AED network were available. Consequently, the actual distribution and the exact number of all AEDs (registered and unregistered) in public and residential locations were unknown. However, the reported number of registered AEDs in this study can only be an underestimation of the actual total number of AEDs disseminated in residential locations. We did not know whether an AED was collected by an OHCA bystander or brought to the site by a non-bystander who was contacted by the emergency medical dispatch center e.g. as a result of local initiatives in rural areas of Denmark where an AED is brought to the arrest site by local first responders.[111,116] However, these limitations do not change our conclusion that no increase in bystander defibrillation in residential locations was observed during the study period.

Geographic data on the exact location of each OHCA were not available. Consequently, it was not possible to estimate the distance between the nearest registered AED and the OHCA site.

5.2 STUDY II

This study was powered to demonstrate feasibility and to examine reactions from a new group of first responders, but the study was not large enough to examine efficacy and cost-benefit. Consequently, the study could not evaluate whether the program had improved OHCA survival.

The survey response rate on questionnaires following OHCA dispatches was overall high. Some of the questionnaires concerned the same OHCA cases from different home care providers who responded. Consequently, answers regarding readiness could be biased because of interdependent answers. Further, we cannot exclude selection bias on answers. However, assuming that all the questionnaire non-responders felt uncomfortable at handling the OHCA situation then approximately 83% of the home care providers felt comfortable.

At the beginning of the study period, the response times reported by the home care providers proved to be inaccurate. Consequently, the reported distances travelled and response times by the home care providers were not collected from the total study period. To validate whether the home care providers arrived before EMS during the study period with inaccurate response time measures, the case files from each dispatch were reviewed.

5.3 STUDY III

Because of the observational design in Study III, the results related to driving distances are only associations and not causal relations. We performed adjusted analyses considering different confounding variables, which did not change our conclusions, but residual confounding related to the different driving distances cannot be excluded. However, if residual confounding was significant in our study the analysis where survival was analyzed according to EMS defibrillation at different driving distances would likely have shown differences in survival. This was not observed, limiting the risk of important residual confounding affecting the results.

Data on the exact position of the firefighters when dispatched to the OHCA cases were not available. Data provided by the Durham Fire Department reported that the firefighters were dispatched from fire stations in most cases. Further, if the firefighter first responders were not in close proximity to the fire stations when dispatched that would average the study results towards the null.

No data on potential police officer first responders were available. To address this potential issue, local EMS authorities were consulted. They confirmed that early

defibrillation provided by police first responders was limited during the study period. In addition, as the police officers are patrolling on the road they are not related to the location of fire stations.

The number of fire stations in the three study counties in North Carolina was high when compared with a typical lower number of fire stations per city in Denmark.[51] A limited number of fire stations with average long driving distances is likely to constrain the benefit of using firefighters as first responders in such communities.

Only fire stations that were staffed 24 hours per day and seven days per week were included in this study. Some communities are covered by volunteer fire departments. In such communities, the fire stations are not consistently staffed 24 hours per day and seven days per week. Consequently, our results do not necessarily apply for those communities, where the optimal coverage distance from nearest fire station might be more limited.

6 CONCLUSIONS

As several initiatives in Denmark were undertaken to facilitate bystander defibrillation, bystander defibrillation rates improved markedly in public locations but remained unchanged and limited in residential locations. Concomitantly, survival increased in both locations. However, the most marked increase in survival was in public locations following bystander defibrillation.

Home care providers in Denmark reported a high degree of preparedness in handling OHCA cases when dispatched as first responders in parallel with EMS personnel. However, several limitations to this approach were observed. In 47% of OHCA cases, the home care providers arrived before EMS. When they arrived before EMS, they performed CPR in 100% of cases, but an AED was only applied in 30% of cases with one shock delivered. A delay between the dispatch of EMS personnel and the home care providers was observed at 2 minutes and 23 seconds potentially constraining the chances of early arrivals.

Survival following firefighter first responder defibrillation in three major counties, North Carolina, USA, was higher at short distances (<1 mile) between the nearest fire station and the OHCA site compared with long distances (>2 miles). The firefighter first responders are dispatched in parallel with EMS personnel to many emergencies and usually no delay between the first responder and EMS personnel dispatches was observed. More OHCAs occurred in a public location in areas with short distance to nearest fire station compared with areas with long distance to fire stations. This study supports efforts to consider the location of first responder units and optimal travel distance when organizing prehospital systems of OHCA care.

7 PERSPECTIVES AND FUTURE RESEARCH

In Study I, initiatives to facilitate bystander defibrillation were associated with a marked increase in bystander defibrillation in public locations. However, no increase in bystander defibrillation was observed in residential locations where most OHCAs occur.[7] Conversely, the home care provider first responders in Study II were most likely to respond to OHCAs in residential locations. Combining the two strategies with onsite AEDs in public high-risk areas, where bystanders are likely to be nearby, with first responder programs in rural and residential areas might prove cost-effective in providing early defibrillation compared with a more comprehensive ambulance coverage. However, little is known about in which exact geographical areas one strategy should be prioritized in favour of the other. Study III estimated the coverage range of a first responder where a limited dispatch delay between EMS personnel and the first responder was observed. Further, the firefighter first responders used a siren when driving. Knowledge on first responder expected coverage ranges are important when organizing prehospital systems of OHCA care. Future studies on first responder programs should focus on examining the effective range of the first responders for varying types of responders in different community settings. In the future, deliverance of AEDs to OHCA sites might be optimized using emerging drone technologies, especially in rural and residential locations of arrest.[117,118]

While Guidelines by the European Resuscitation Council recommend placing AEDs in areas where more than 1 OHCA per 5 years occur, many AEDs are placed without systematically considering area characteristics, including Study I.[18,23,85] When AED placements are unguided but based on local or political initiatives, paradox placements of AEDs in locations with low chances of an OHCA occurring nearby have been described.[28] Future studies examining where the AEDs in the Danish AED registry are located and where to actually place AEDs in different areas are important to elaborate whether AEDs are actually available in high-risk areas and improve the provision of early defibrillation further while maintaining cost effectiveness.[119] A previous study examined whether mathematical optimization using straight-line distances could improve coverage in an urban environment.[120] The study stated, that by using mathematical models to identify clusters of OHCAs it was possible to optimize AED placements and improve OHCA coverage rates. However, the study assumed a coverage area of only a 100m radius from the AEDs. Not surprisingly, wider coverage AED distance assumptions decreases the number of required AEDs to provide AED coverage.[121] However, as the coverage distance increases it takes more time to collect the AED which likely decreases the chances of early defibrillation. Little is known about the association between the actual walking distance of a nearby available AED and chances of early defibrillation, which is of paramount importance when constructing models to optimize the placement of AEDs

in local communities. Further, the coverage range might differ according to factors characterizing different public areas such as the average number of expected bystanders present, whether dispatcher-assisted guidance to nearest AED is available, the distribution of OHCAs during day and night time, availability of placed AEDs, and the type of environment (e.g. urban areas are likely to have different infrastructure than suburban and rural areas).[28,29,38,122–124] Further, advances in the understanding of the difference in using the Euclidian distance assumptions compared with actual walking/driving distances should be made when attempting optimization of onsite AED placements in communities. High-risk OHCA areas are usually identified using retrospective data based on the assumption that OHCAs in the future are likely to occur in the same locations as in the past.[18,29] However, community characteristics are likely to change over time[125], which could challenge these assumptions and make optimization of placing AEDs in communities a dynamic process over time.

When organizing first responder programs, focus should be made on decreasing the delay before the dispatch of the first responders compared with EMS personnel to achieve high first-arrival rates for the first responders. Considerations regarding which emergencies the first responders should be dispatched to are important as discussed for Study II and Study III. However, if the first responder dispatch criteria are widened beyond high-suspicion OHCA cases, many dispatches to non-OHCA situations should be anticipated. Increasing the first responder dispatch options to include assisting at other medical emergencies than OHCAs could be valuable in pursuing this goal, especially in rural locations where the incidence of OHCAs is low.

While early defibrillation is important for survival after OHCA, weaknesses in other parts of the chain of survival are likely to diminish the effect of early defibrillation.[18] When CPR is not promptly initiated after onset of arrest, chances of defibrillation and subsequent survival decreases.[126,127] In recent years, bystander CPR rates have increased in many countries.[7,8,24–27] Continuous efforts to increase the bystander CPR rates further are important to improve OHCA survival rates further. After ROSC has been achieved, the risk of recurrent arrest is high.[128,129] Optimal advanced post-resuscitation care such as securing optimal ventilation of OHCA patients, and advanced treatments such as early revascularization are important to sustain ROSC, improve survival, and favorable cognitive outcomes.[130] Establishing and maintaining a strong OHCA care system in both prehospital and hospital settings should be a strong priority to improve survival of OHCA patients in the future.

8 REFERENCES

1. Jacobs I, Nadkarni V, Bahr J, et al. Cardiac arrest and cardiopulmonary resuscitation outcome reports: update and simplification of the Utstein templates for resuscitation registries. A statement for healthcare professionals from a task force of the international liaison committee on resuscitation (American Heart Association, European Resuscitation Council, Australian Resuscitation Council, New Zealand Resuscitation Council, Heart and Stroke Foundation of Canada, InterAmerican Heart Foundation, Resuscitation Council of Southern Africa). *Resuscitation*. 2004;63(3):233-249. doi:10.1016/j.resuscitation.2004.09.008.

2. Cummins RO, Chamberlain DA, Abramson NS, et al. Recommended guidelines for uniform reporting of data from out-of-hospital cardiac arrest: the Utstein Style. A statement for health professionals from a task force of the American Heart Association, the European Resuscitation Council, the Heart and Stroke. *Circulation*. 1991;84(2):960-975. doi:10.1161/01.CIR.84.2.960.

3. Gräsner J-T, Lefering R, Koster RW, et al. EuReCa ONE-27 Nations, ONE Europe, ONE Registry: A prospective one month analysis of out-of-hospital cardiac arrest outcomes in 27 countries in Europe. *Resuscitation*. 2016;105:188-195. doi:10.1016/j.resuscitation.2016.06.004.

4. Writing Group Members, Mozaffarian D, Benjamin EJ, et al. Heart Disease and Stroke Statistics-2016 Update: A Report From the American Heart Association. *Circulation*. 2016;133(4):e38-360. doi:10.1161/CIR.0000000000000350.

5. Cummins RO, Ornato JP, Thies WH, Pepe PE. Improving survival from sudden cardiac arrest: the “chain of survival” concept. A statement for health professionals from the Advanced Cardiac Life Support Subcommittee and the Emergency Cardiac Care Committee, American Heart Association. *Circulation*. 1991;83(5):1832-1847. doi:10.1161/01.CIR.83.5.1832.

6. Monsieurs KG, Nolan JP, Bossaert LL, et al. European Resuscitation Council Guidelines for Resuscitation 2015: Section 1. Executive summary. *Resuscitation*. 2015;95:1-80. doi:10.1016/j.resuscitation.2015.07.038.

7. Wissenberg M, Lippert FK, Folke F, et al. Association of national initiatives to improve cardiac arrest management with rates of bystander intervention and patient survival after out-of-hospital cardiac arrest. *JAMA*. 2013;310(13):1377-1384. doi:10.1001/jama.2013.278483.

8. Hasselqvist-Ax I, Riva G, Herlitz J, et al. Early cardiopulmonary resuscitation in out-of-hospital cardiac arrest. *The New England journal of medicine*. 2015;372(24):2307-2315. doi:10.1056/NEJMoa1405796.

9. Caffrey SL, Willoughby PJ, Pepe PE, Becker LB. Public use of automated external defibrillators. *The New England journal of medicine*. 2002;347(16):1242-1247. doi:10.1056/NEJMoa020932.

10. Page RL, Joglar JA, Kowal RC, et al. Use of automated external defibrillators by a U.S. airline. *The New England journal of medicine*. 2000;343(17):1210-1216. doi:10.1056/NEJM200010263431702.

11. Valenzuela TD, Roe DJ, Nichol G, Clark LL, Spaite DW, Hardman RG. Outcomes of rapid defibrillation by security officers after cardiac arrest in casinos. *The New England journal of medicine*. 2000;343(17):1206-1209. doi:10.1056/NEJM200010263431701.

12. Nielsen AM, Folke F, Lippert FK, Rasmussen LS. Use and benefits of public access defibrillation in a nation-wide network. *Resuscitation*. 2013;84(4):430-434. doi:10.1016/j.resuscitation.2012.11.008.

13. Weisfeldt ML, Becker LB. Resuscitation after cardiac arrest: a 3-phase time-sensitive model. *JAMA*. 2002;288(23):3035-3038. doi:10.1001/jama.288.23.3035.

14. Hansen CM, Kragholm K, Granger CB, et al. The role of bystanders, first responders, and emergency medical service providers in timely defibrillation and related outcomes after out-of-hospital cardiac arrest: Results from a statewide registry. *Resuscitation*. 2015;96:303-309. doi:10.1016/j.resuscitation.2015.09.002.

15. Gold LS, Fahrenbruch CE, Rea TD, Eisenberg MS. The relationship between time to arrival of emergency medical services (EMS) and survival from out-of-hospital ventricular fibrillation cardiac arrest. *Resuscitation*. 2010;81(5):622-625. doi:10.1016/j.resuscitation.2010.02.004.

16. Hallstrom AP, Ornato JP, Weisfeldt M, et al. Public-access defibrillation and survival after out-of-hospital cardiac arrest. *The New England journal of medicine*. 2004;351(7):637-646. doi:10.1056/NEJMoa040566.

17. Yeung J, Okamoto D, Soar J, Perkins GD. AED training and its impact on skill acquisition, retention and performance--a systematic review of alternative training methods. *Resuscitation*. 2011;82(6):657-664. doi:10.1016/j.resuscitation.2011.02.035.

18. Perkins GD, Handley AJ, Koster RW, et al. European Resuscitation Council Guidelines for Resuscitation 2015: Section 2. Adult basic life support and automated external defibrillation. *Resuscitation*. 2015;95:81-99. doi:10.1016/j.resuscitation.2015.07.015.

19. Koster RW, Baubin MA, Bossaert LL, et al. European Resuscitation Council Guidelines for Resuscitation 2010 Section 2. Adult basic life support and use of automated external defibrillators. *Resuscitation*. 2010;81(10):1277-1292. doi:10.1016/j.resuscitation.2010.08.009.

20. Link MS, Atkins DL, Passman RS, et al. Part 6: electrical therapies: automated external defibrillators, defibrillation, cardioversion, and pacing: 2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. *Circulation*. 2010;122(18 Suppl 3):S706-19. doi:10.1161/CIRCULATIONAHA.110.970954.

21. Hazinski MF, Idris AH, Kerber RE, et al. Lay rescuer automated external defibrillator ("public access defibrillation") programs: lessons learned from an international multicenter trial: advisory statement from the American Heart Association Emergency Cardiovascular Committee; the Council on Cardiopulmonary, Perioperative, and Critical Care; and the Council on Clinical Cardiology. *Circulation*. 2005;111(24):3336-3340. doi:10.1161/CIRCULATIONAHA.105.165674.

22. Fleischhackl R, Roessler B, Domanovits H, et al. Results from Austria's nationwide public access defibrillation (ANPAD) programme collected over 2 years. *Resuscitation*. 2008;77(2):195-200. doi:10.1016/j.resuscitation.2007.11.019.

23. Kitamura T, Kiyohara K, Sakai T, et al. Public-Access Defibrillation and Out-of-Hospital Cardiac Arrest in Japan. *New England Journal of Medicine*. 2016;375(17):1649-1659. doi:10.1056/NEJMsa1600011.

24. Graham R, Mccoy MA, Schultz AM. Strategies to Improve Cardiac Arrest Survival : A Time to Act. http://iom.nationalacademies.org/Reports/2015/Strategies-to-Improve-Cardiac-Arrest-Survival.aspx. Published 2015. Accessed September 1, 2016.

25. Chan PS, McNally B, Tang F, Kellermann a. Recent Trends in Survival From Out-of-Hospital Cardiac Arrest in the United States. *Circulation*. 2014;130(21):1876-1882. doi:10.1161/CIRCULATIONAHA.114.009711.

26. Daya MR, Schmicker RH, Zive DM, et al. Out-of-hospital cardiac arrest

survival improving over time: Results from the Resuscitation Outcomes Consortium (ROC). *Resuscitation*. 2015;91:108-115. doi:10.1016/j.resuscitation.2015.02.003.

27. Deakin CD, Shewry E, Gray HH. Public access defibrillation remains out of reach for most victims of out-of-hospital sudden cardiac arrest. *Heart (British Cardiac Society)*. 2014;100(8):619-623. doi:10.1136/heartjnl-2013-305030.

28. Folke F, Lippert FK, Nielsen SL, et al. Location of cardiac arrest in a city center: strategic placement of automated external defibrillators in public locations. *Circulation*. 2009;120(6):510-517. doi:10.1161/CIRCULATIONAHA.108.843755.

29. Hansen CM, Wissenberg M, Weeke P, et al. Automated external defibrillators inaccessible to more than half of nearby cardiac arrests in public locations during evening, nighttime, and weekends. *Circulation*. 2013;128(20):2224-2231. doi:10.1161/CIRCULATIONAHA.113.003066.

30. Brooks B, Chan S, Lander P, Adamson R, Hodgetts G a., Deakin CD. Public knowledge and confidence in the use of public access defibrillation. *Heart (British Cardiac Society)*. 2015;101(12):967-971. doi:10.1136/heartjnl-2015-307624.

31. Murakami Y, Iwami T, Kitamura T, et al. Outcomes of out-of-hospital cardiac arrest by public location in the public-access defibrillation era. *Journal of the American Heart Association*. 2014;3(2):e000533. doi:10.1161/JAHA.113.000533.

32. Leung AC, Asch DA, Lozada KN, et al. Where are lifesaving automated external defibrillators located and how hard is it to find them in a large urban city? *Resuscitation*. 2013;84(7):910-914. doi:10.1016/j.resuscitation.2013.01.010.

33. Bardy GH, Lee KL, Mark DB, et al. Home use of automated external defibrillators for sudden cardiac arrest. *The New England journal of medicine*. 2008;358(17):1793-1804. doi:10.1056/NEJMoa0801651.

34. Merchant RM, Asch D a. Can you find an automated external defibrillator if a life depends on it? *Circulation Cardiovascular quality and outcomes*. 2012;5(2):241-243. doi:10.1161/CIRCOUTCOMES.111.964825.

35. Aufderheide T, Hazinski MF, Nichol G, et al. Community lay rescuer automated external defibrillation programs: key state legislative components

and implementation strategies: a summary of a decade of experience for healthcare providers, policymakers, legislators, employers, and community leaders fro. *Circulation*. 2006;113(9):1260-1270. doi:10.1161/CIRCULATIONAHA.106.172289.

36. Folke F, Gislason GH, Lippert FK, et al. Differences between out-of-hospital cardiac arrest in residential and public locations and implications for public-access defibrillation. *Circulation*. 2010;122(6):623-630. doi:10.1161/CIRCULATIONAHA.109.924423.

37. Weisfeldt ML, Everson-Stewart S, Sitlani C, et al. Ventricular tachyarrhythmias after cardiac arrest in public versus at home. *The New England journal of medicine*. 2011;364(4):313-321. doi:10.1056/NEJMoa1010663.

38. Hansen CM, Lippert FK, Wissenberg M, et al. Temporal Trends in Coverage of Historical Cardiac Arrests Using a Volunteer-Based Network of Automated External Defibrillators Accessible to Laypersons and Emergency Dispatch Centers. *Circulation*. 2014;130(21):1859-1867. doi:10.1161/CIRCULATIONAHA.114.008850.

39. Zijlstra J a, Stieglis R, Riedijk F, Smeekes M, van der Worp WE, Koster RW. Local lay rescuers with AEDs, alerted by text messages, contribute to early defibrillation in a Dutch out-of-hospital cardiac arrest dispatch system. *Resuscitation*. 2014;85(11):1444-1449. doi:10.1016/j.resuscitation.2014.07.020.

40. Malta Hansen C, Kragholm K, Pearson D a., et al. Association of Bystander and First responder Intervention With Survival After Out-of-Hospital Cardiac Arrest in North Carolina, 2010-2013. *Jama*. 2015;314(3):255. doi:10.1001/jama.2015.7938.

41. Blom MT, Beesems SG, Homma PCM, et al. Improved Survival After Out-of-Hospital Cardiac Arrest and Use of Automated External Defibrillators. *Circulation*. 2014;130(21):1868-1875. doi:10.1161/CIRCULATIONAHA.114.010905.

42. Ringh M, Rosenqvist M, Hollenberg J, et al. Mobile-phone dispatch of laypersons for CPR in out-of-hospital cardiac arrest. *The New England journal of medicine*. 2015;372(24):2316-2325. doi:10.1056/NEJMoa1406038.

43. Ströhle M, Paal P, Strapazzon G, Avancini G, Procter E, Brugger H. Defibrillation in rural areas. *The American journal of emergency medicine*.

August 2014:1-5. doi:10.1016/j.ajem.2014.08.046.

44. Moore MJ, Hamilton AJ, Cairns KJ, et al. The Northern Ireland Public Access Defibrillation (NIPAD) study: effectiveness in urban and rural populations. *Heart (British Cardiac Society)*. 2008;94(12):1614-1619. doi:10.1136/hrt.2007.130534.

45. Capucci A, Aschieri D, Piepoli MF, Bardy GH, Iconomu E, Arvedi M. Tripling survival from sudden cardiac arrest via early defibrillation without traditional education in cardiopulmonary resuscitation. *Circulation*. 2002;106(9):1065-1070. doi:10.1161/01.CIR.0000028148.62305.69.

46. Hollenberg J, Riva G, Bohm K, et al. Dual dispatch early defibrillation in out-of-hospital cardiac arrest: the SALSA-pilot. *European heart journal*. 2009;30(14):1781-1789. doi:10.1093/eurheartj/ehp177.

47. Saner H, Morger C, Eser P, von Planta M. Dual dispatch early defibrillation in out-of-hospital cardiac arrest in a mixed urban-rural population. *Resuscitation*. 2013;84(9):1197-1202. doi:10.1016/j.resuscitation.2013.02.023.

48. Becker L, Husain S, Kudenchuk P, Doll A, Rea T, Eisenberg M. Treatment of cardiac arrest with rapid defibrillation by police in King County, Washington. *Prehospital emergency care : official journal of the National Association of EMS Physicians and the National Association of State EMS Directors*. 2013;18(1):22-27. doi:10.3109/10903127.2013.825353.

49. Husain S, Eisenberg M. Police AED programs: a systematic review and meta-analysis. *Resuscitation*. 2013;84(9):1184-1191. doi:10.1016/j.resuscitation.2013.03.040.

50. van Alem AP, Vrenken RH, de Vos R, Tijssen JGP, Koster RW. Use of automated external defibrillator by first responders in out of hospital cardiac arrest: prospective controlled trial. *BMJ (Clinical research ed)*. 2003;327(7427):1312. doi:10.1136/bmj.327.7427.1312.

51. Høyer CB, Christensen EF. Fire fighters as basic life support responders: a study of successful implementation. *Scandinavian journal of trauma, resuscitation and emergency medicine*. 2009;17:16. doi:10.1186/1757-7241-17-16.

52. Brøndum S, Thomas G, Faurbye N, Kvist B, Lindberg J, Hansen PA. Home care personnel as first responders in a rural area of Denmark. *Resuscitation*. 2014;84:S2. doi:10.1016/j.resuscitation.2013.08.021.

53. Statistics Denmark. http://www.statistikbanken.dk/statbank5a/default.asp?w=1920. Accessed February 1, 2016.

54. Sundhedsstyrelsen. Automated external defibrillators (AED) placed outside hospital, 2011 (in danish). Danish Health and Medicines Authority web site. http://sundhedsstyrelsen.dk/publ/Publ2011/SYB/Hjertestarter/AEDhjertestarter.pdf. Accessed February 1, 2016.

55. The Danish foundation TrygFonden. Hjertestarter.dk. https://www.hjertestarter.dk/Service-Pages/InEnglish. Accessed September 1, 2016.

56. Erhvervsstyrelsen. PlansystemDK. https://erhvervsstyrelsen.dk/plansystemdk. Accessed November 29, 2016.

57. Daniel RM, Cousens SN, De Stavola BL, Kenward MG, Sterne JAC. Methods for dealing with time-dependent confounding. *Statistics in medicine*. 2013;32(9):1584-1618. doi:10.1002/sim.5686.

58. Hernán, MA. Robins J. *Causal Inference*. Boca Raton: Chapman & Hall/CRC, forthcoming; 2016. http://www.hsph.harvard.edu/miguel-hernan/causal-inference-book/.

59. Buuren S van, Groothuis-Oudshoorn K. mice: Multivariate Imputation by Chained Equations in R. *Journal of Statistical Software*. 2011;45(3):67. http://www.jstatsoft.org/v45/i03.

60. Kabacoff RI. *R IN ACTION: Data Analysis and Graphics with R*.; 2011. doi:citeulike-article-id:10054678.

61. Newman D a. Missing Data: Five Practical Guidelines. *Organizational Research Methods*. 2014;17(4):372-411. doi:10.1177/1094428114548590.

62. Graham JW, Olchowski AE, Gilreath TD. How many imputations are really needed? Some practical clarifications of multiple imputation theory. *Prevention Science*. 2007;8(3):206-213. doi:10.1007/s11121-007-0070-9.

63. R Core Team. R: A Language and Environment for Statistical Computing. 2015. http://www.r-project.org/.

64. Rasmussen SR, Aaløkke S. *Hjertestart I Frederikshavn Kommune Evaluering Af Intervention Med Udkald Af Hjemmeplejens*. http://loader.goernogetforhjertet.dk//files/parattilhjertestart/Hjertestart i

Frederikshavn Kommune.pdf.

65. Nolan JP, Soar J, Zideman DA, et al. European Resuscitation Council Guidelines for Resuscitation 2010 Section 1 . Executive summary. 2010;81:1219-1276. doi:10.1016/j.resuscitation.2010.08.021.

66. McNally B, Robb R, Mehta M, et al. Out-of-hospital cardiac arrest surveillance --- Cardiac Arrest Registry to Enhance Survival (CARES), United States, October 1, 2005--December 31, 2010. *Morbidity and mortality weekly report Surveillance summaries (Washington, DC : 2002)*. 2011;60(8):1-19. doi:ss6008a1 [pii].

67. Fosbøl EL, Dupre ME, Strauss B, et al. Association of neighborhood characteristics with incidence of out-of-hospital cardiac arrest and rates of bystander-initiated CPR: Implications for community-based education intervention. *Resuscitation*. 2014;85(11):1512-1517. doi:10.1016/j.resuscitation.2014.08.013.

68. United States Census Bureau. American FactFinder. https://factfinder.census.gov/faces/nav/jsf/pages/index.xhtml. Accessed February 9, 2017.

69. McNally B, Stokes A, Crouch A, Kellermann AL, CARES Surveillance Group. CARES: Cardiac Arrest Registry to Enhance Survival. *Annals of emergency medicine*. 2009;54(5):674-683.e2. doi:10.1016/j.annemergmed.2009.03.018.

70. Shah MN. The formation of the emergency medical services system. *American journal of public health*. 2006;96(3):414-423. doi:10.2105/AJPH.2004.048793.

71. Blanchard IE, Doig CJ, Hagel BE, et al. Emergency medical services response time and mortality in an urban setting. *Prehospital emergency care : official journal of the National Association of EMS Physicians and the National Association of State EMS Directors*. 2012;16(1):142-151. doi:10.3109/10903127.2011.614046.

72. McNally B. Cardiac Arrest Registry to Enhance Survival - CARES Complete Data Set for EMS, Hospital, and CAD Participants and Instructions for Abstracting and Coding Data Elements. https://mycares.net/downloads/Data Dictionary (2013).pdf. Published 2013. Accessed June 1, 2017.

73. National Fire Protection Association. NFPA 1710, Standard for the

Organization and Deployment of Fire Suppression Operations, Emergency Medical Operations, and Special Operations to the Public by Career Fire Departments. http://www.nfpa.org/codes-and-standards/all-codes-and-standards/list-of-codes-and-standards/detail?code=1710. Published 2010. Accessed June 1, 2017.

74. ISO. Fire Suppression Rating Schedule. https://www.isomitigation.com/fsrs/fire-suppression-rating-schedule-fsrs-overview.html. Accessed June 1, 2017.

75. United States Census Bureau. Geographic Terms and Concepts - Census Tract. https://www.census.gov/geo/reference/gtc/gtc_ct.html. Published 2012. Accessed February 9, 2017.

76. United States Census Bureau. American Community Survey (ACS). https://www.census.gov/programs-surveys/acs/about.html. Accessed February 9, 2017.

77. Jennett B, Bond M. Assessment of outcome after severe brain damage. *Lancet (London, England)*. 1975;1(7905):480-484. http://www.ncbi.nlm.nih.gov/pubmed/46957.

78. Nielsen N, Wetterslev J, Cronberg T, et al. Targeted temperature management at 33°C versus 36°C after cardiac arrest. *The New England journal of medicine*. 2013;369(23):2197-2206. doi:10.1056/NEJMoa1310519.

79. Esri. ArcGis. http://www.esri.com/arcgis/about-arcgis. Accessed May 3, 2017.

80. Esri. Esri Network Analyst. http://www.esri.com/software/arcgis/extensions/networkanalyst. Accessed February 10, 2017.

81. Esri. Esri Business Analyst. http://www.esri.com/software/businessanalyst. Accessed January 12, 2016.

82. Proctor BD, Semega JL, Kollar MA. Income and Poverty in the United States : 2015 Current Population Reports. *Current Population Reports*. 2016;P60-256(RV(September):59. doi:Retrieved from http://www.census.gov/content/dam/Census/library/publications/2016/demo/p60-256.pdf.

83. U.S. Department of Health & Human Services. Poverty Guidelines.

https://aspe.hhs.gov/poverty-guidelines. Accessed May 31, 2017.

84. Kitamura T, Iwami T, Kawamura T, Nagao K, Tanaka H, Hiraide A. Nationwide public-access defibrillation in Japan. *The New England journal of medicine*. 2010;362(11):994-1004. doi:10.1056/NEJMoa0906644.

85. Lijovic M, Bernard S, Nehme Z, Walker T, Smith K. Public access defibrillation—Results from the Victorian Ambulance Cardiac Arrest Registry. *Resuscitation*. October 2014:1-6. doi:10.1016/j.resuscitation.2014.10.005.

86. Ringh M, Jonsson M, Nordberg P, et al. Survival after Public Access Defibrillation in Stockholm, Sweden--A striking success. *Resuscitation*. 2015;91:1-7. doi:10.1016/j.resuscitation.2015.02.032.

87. Renkiewicz GK, Hubble MW, Wesley DR, et al. Probability of a shockable presenting rhythm as a function of EMS response time. *Prehospital emergency care : official journal of the National Association of EMS Physicians and the National Association of State EMS Directors*. 2014;18(2):224-230. doi:10.3109/10903127.2013.851308.

88. Herlitz J, Svensson L, Engdahl J, Silfverstolpe J. Characteristics and outcome in out-of-hospital cardiac arrest when patients are found in a non-shockable rhythm. *Resuscitation*. 2008;76(1):31-36. doi:10.1016/j.resuscitation.2007.06.027.

89. Wissenberg M, Folke F, Hansen CM, et al. Survival After Out-of-Hospital Cardiac Arrest in Relation to Age and Early Identification of Patients With Minimal Chance of Long-Term Survival. *Circulation*. 2015;131(18):1536-1545. doi:10.1161/CIRCULATIONAHA.114.013122.

90. Wissenberg M, Hansen CM, Folke F, et al. Survival after out-of-hospital cardiac arrest in relation to sex: A nationwide registry-based study. *Resuscitation*. 2014;85(9):1212-1218. doi:10.1016/j.resuscitation.2014.06.008.

91. Hansen SM, Wissenberg M, Rajan S, et al. Sammenfatning af resultater fra Dansk Hjertestopregister 2001-2012. http://www.svoem.org/_files/_database/database105/trygfonden_2014-10-17.pdf. Published 2014. Accessed September 1, 2016.

92. Waalewijn RA, Tijssen JGP, Koster RW. Bystander initiated actions in out-of-hospital cardiopulmonary resuscitation: Results from the Amsterdam Resuscitation Study (ARRESUST). *Resuscitation*. 2001;50:273-279.

doi:10.1016/S0300-9572(01)00354-9.

93. Tanigawa K, Iwami T, Nishiyama C, Nonogi H, Kawamura T. Are trained individuals more likely to perform bystander CPR? An observational study. *Resuscitation*. 2011;82(5):523-528. doi:10.1016/j.resuscitation.2011.01.027.

94. Sunde K, Pytte M, Jacobsen D, et al. Implementation of a standardised treatment protocol for post resuscitation care after out-of-hospital cardiac arrest. *Resuscitation*. 2007;73(1):29-39. doi:10.1016/j.resuscitation.2006.08.016.

95. Weisfeldt ML, Sitlani CM, Ornato JP, et al. Survival after application of automatic external defibrillators before arrival of the emergency medical system: evaluation in the resuscitation outcomes consortium population of 21 million. *Journal of the American College of Cardiology*. 2010;55(16):1713-1720. doi:10.1016/j.jacc.2009.11.077.

96. Rajan S, Wissenberg M, Folke F, et al. Association of Bystander Cardiopulmonary Resuscitation and Survival According to Ambulance Response Times After Out-of-Hospital Cardiac Arrest. *Circulation*. 2016;134(25):2095-2104. doi:10.1161/CIRCULATIONAHA.116.024400.

97. Lerner EB, Hinchey PR, Billittier AJ. A survey of first responder firefighters' attitudes, opinions, and concerns about their automated external defibrillator program. *Prehospital emergency care : official journal of the National Association of EMS Physicians and the National Association of State EMS Directors*. 2000;7(1):120-124. http://www.ncbi.nlm.nih.gov/pubmed/12540155. Accessed November 12, 2014.

98. Prina LD, White RD, Atkinson EJ. Automated external defibrillators and first responders: a satisfaction survey. *Resuscitation*. 2002;53(2):171-177. http://www.ncbi.nlm.nih.gov/pubmed/12009221. Accessed November 14, 2014.

99. Rørtveit S, Meland E. First responder resuscitation teams in a rural Norwegian community: sustainability and self-reports of meaningfulness, stress and mastering. *Scandinavian journal of trauma, resuscitation and emergency medicine*. 2010;18:25. doi:10.1186/1757-7241-18-25.

100. Kuramoto N, Morimoto T, Kubota Y, et al. Public perception of and willingness to perform bystander CPR in Japan. *Resuscitation*. 2008;79(3):475-481. doi:10.1016/j.resuscitation.2008.07.005.

101. Greif R, Lockey AS, Conaghan P, et al. European Resuscitation Council Guidelines for Resuscitation 2015: Section 10. Education and implementation of resuscitation. *Resuscitation*. 2015;95:288-301. doi:10.1016/j.resuscitation.2015.07.032.

102. Duke University EMS. EMT Basic Class. http://dukeems.org/emt-training/. Accessed May 3, 2017.

103. NCDOI Office of State Fire Marshal. NC Fire Fighter Certification. http://www.ncdoi.com/OSFM/Fire_Rescue_Commission/Default.aspx?field1=Certification_and_Training_-_NC_Fire_Fighter_Certification&user=Certification_and_Training. Accessed May 3, 2017.

104. North Carolina Department of Insurance Office of State Fire Marshall. Certification and Training - NC Fire Fighter Certification. http://www.ncdoi.com/OSFM/Fire_Rescue_Commission/Default.aspx?field1=Certification_and_Training_-_NC_Fire_Fighter_Certification&user=Certification_and_Training. Accessed February 14, 2017.

105. Ringh M, Fredman D, Nordberg P, Stark T, Hollenberg J. Mobile phone technology identifies and recruits trained citizens to perform CPR on out-of-hospital cardiac arrest victims prior to ambulance arrival. *Resuscitation*. 2011;82(12):1514-1518. doi:10.1016/j.resuscitation.2011.07.033.

106. Myerburg RJ, Fenster J, Velez M, et al. Impact of community-wide police car deployment of automated external defibrillators on survival from out-of-hospital cardiac arrest. *Circulation*. 2002;106(9):1058-1064. doi:10.1161/01.CIR.0000028147.92190.A7.

107. Groh WJ, Newman MM, Beal PE, Fineberg NS, Zipes DP. Limited response to cardiac arrest by police equipped with automated external defibrillators: lack of survival benefit in suburban and rural Indiana--the police as responder automated defibrillation evaluation (PARADE). *Academic emergency medicine : official journal of the Society for Academic Emergency Medicine*. 2001;8(4):324-330. http://www.ncbi.nlm.nih.gov/pubmed/11282666. Accessed November 10, 2014.

108. Waalewijn RA, Nijpels MA, Tijssen JG, Koster RW. Prevention of deterioration of ventricular fibrillation by basic life support during out-of-hospital cardiac arrest. *Resuscitation*. 2002;54(1):31-36. doi:10.1016/S0300-9572(02)00047-3.

109. Lewis M, Stubbs BA, Eisenberg MS. Dispatcher-assisted cardiopulmonary resuscitation: Time to identify cardiac arrest and deliver chest compression instructions. *Circulation*. 2013;128(14):1522-1530. doi:10.1161/CIRCULATIONAHA.113.002627.

110. Travers S, Jost D, Gillard Y, et al. Out-of-hospital cardiac arrest phone detection: Those who most need chest compressions are the most difficult to recognize. *Resuscitation*. 2014;85(12):1720-1725. doi:10.1016/j.resuscitation.2014.09.020.

111. Henriksen FL, Schorling P, Hansen B, Schakow H, Larsen ML. FirstAED emergency dispatch, global positioning of community first responders with distinct roles - a solution to reduce the response times and ensuring an AED to early defibrillation in the rural area Langeland. *International Journal of Networking and Virtual Organisations*. 2016;16(1):86. doi:10.1504/IJNVO.2016.075131.

112. Strömsöe A, Svensson L, Claesson A, Lindkvist J, Lundström A, Herlitz J. Association between population density and reported incidence, characteristics and outcome after out-of-hospital cardiac arrest in Sweden. *Resuscitation*. 2011;82(10):1307-1313. doi:10.1016/j.resuscitation.2011.04.025.

113. Yasunaga H, Miyata H, Horiguchi H, et al. Population density, call-response interval, and survival of out-of-hospital cardiac arrest. *International journal of health geographics*. 2011;10(1):26. doi:10.1186/1476-072X-10-26.

114. Hansen SM, Brøndum S, Thomas G, et al. Home Care Providers to the Rescue: A Novel First responder Programme. *PloS one*. 2015;10(10):e0141352. doi:10.1371/journal.pone.0141352.

115. Agerskov M, Nielsen AM, Hansen CM, et al. Public Access Defibrillation: Great benefit and potential but infrequently used. *Resuscitation*. 2015;96:53-58. doi:10.1016/j.resuscitation.2015.07.021.

116. Region Syddanmark. Udbud af udkaldssystem til akuthjælperordninger. https://www.regionsyddanmark.dk/dwn410484. Accessed March 3, 2017.

117. Claesson A, Fredman D, Svensson L, et al. Unmanned aerial vehicles (drones) in out-of-hospital-cardiac-arrest. *Scandinavian journal of trauma, resuscitation and emergency medicine*. 2016;24(1):124. doi:10.1186/s13049-016-0313-5.

118. Boutilier JJ, Brooks SC, Janmohamed A, et al. Optimizing a Drone Network

to Deliver Automated External Defibrillators. *Circulation*. March 2017:CIRCULATIONAHA.116.026318. doi:10.1161/CIRCULATIONAHA.116.026318.

119. Moran PS, Teljeur C, Masterson S, O'Neill M, Harrington P, Ryan M. Cost-effectiveness of a national public access defibrillation programme. *Resuscitation*. 2015;91:48-55. doi:10.1016/j.resuscitation.2015.03.017.

120. Chan TCY, Li H, Lebovic G, et al. Identifying locations for public access defibrillators using mathematical optimization. *Circulation*. 2013;127(17):1801-1809. doi:10.1161/CIRCULATIONAHA.113.001953.

121. Siddiq AA, Brooks SC, Chan TCY. Modeling the impact of public access defibrillator range on public location cardiac arrest coverage. *Resuscitation*. 2013;84(7):904-909. doi:10.1016/j.resuscitation.2012.11.019.

122. Karlsson LIM, Wissenberg M, Fosbøl EL, et al. Diurnal variations in incidence and outcome of out-of-hospital cardiac arrest including prior comorbidity and pharmacotherapy: A nationwide study in Denmark. *Resuscitation*. 2014;85(9):1161-1168. doi:10.1016/j.resuscitation.2014.06.012.

123. Marijon E, Bougouin W, Tafflet M, et al. Population movement and sudden cardiac arrest location. *Circulation*. 2015;131(18):1546-1554. doi:10.1161/CIRCULATIONAHA.114.010498.

124. Brooks SC, Hsu JH, Tang SK, Jeyakumar R, Chan TCY. Determining risk for out-of-hospital cardiac arrest by location type in a Canadian urban setting to guide future public access defibrillator placement. *Annals of emergency medicine*. 2013;61(5):530-538.e2. doi:10.1016/j.annemergmed.2012.10.037.

125. Du P, Coles FB, O'Campo P, McNutt L-A. Changes in population characteristics and their implication on public health research. *Epidemiologic perspectives & innovations : EP+I*. 2007;4:6. doi:10.1186/1742-5573-4-6.

126. Valenzuela TD, Roe DJ, Cretin S, Spaite DW, Larsen MP. Estimating effectiveness of cardiac arrest interventions: a logistic regression survival model. *Circulation*. 1997;96(10):3308-3313. http://www.ncbi.nlm.nih.gov/pubmed/9396421.

127. Larsen MP, Eisenberg MS, Cummins RO, Hallstrom AP. Predicting survival from out-of-hospital cardiac arrest: A graphic model. *Annals of Emergency*

Medicine. 1993;22(11):1652-1658. doi:10.1016/S0196-0644(05)81302-2.

128. Salcido DD, Stephenson AM, Condle JP, Callaway CW, Menegazzi JJ. Incidence of rearrest after return of spontaneous circulation in out-of-hospital cardiac arrest. *Prehospital emergency care : official journal of the National Association of EMS Physicians and the National Association of State EMS Directors*. 2010;14(4):413-418. doi:10.3109/10903127.2010.497902.

129. Koster RW, Walker RG, Chapman FW. Recurrent ventricular fibrillation during advanced life support care of patients with prehospital cardiac arrest. *Resuscitation*. 2008;78(3):252-257. doi:10.1016/j.resuscitation.2008.03.231.

130. Nolan JP, Soar J, Cariou A, et al. European Resuscitation Council and European Society of Intensive Care Medicine Guidelines for Post-resuscitation Care 2015: Section 5 of the European Resuscitation Council Guidelines for Resuscitation 2015. *Resuscitation*. 2015;95:202-222. doi:10.1016/j.resuscitation.2015.07.018.

9 APPENDICES

- **Paper I:**
  Bystander Defibrillation for Out-of-Hospital Cardiac Arrest in Public vs Residential Locations.

- **Paper II:**
  Home Care Providers to the Rescue: A Novel First responder Programme

- **Paper III:**
  The association between driving distance from nearest fire station and survival of out-of-hospital cardiac arrest following early defibrillation by first responders

JAMA Cardiology | Original Investigation

Bystander Defibrillation for Out-of-Hospital Cardiac Arrest in Public vs Residential Locations

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IMPORTANCE Bystander-delivered defibrillation (hereinafter referred to as bystander defibrillation) of patients with out-of-hospital cardiac arrests (OHCAs) remains limited despite the widespread dissemination of automated external defibrillators (AEDs).

OBJECTIVE To examine calendar changes in bystander defibrillation and subsequent survival according to a public or a residential location of the cardiac arrest after nationwide initiatives in Denmark to facilitate bystander-mediated resuscitative efforts, including bystander defibrillation.

DESIGN, SETTING, AND PARTICIPANTS This nationwide study identified 18 688 patients in Denmark with first-time OHCA from June 1, 2001, to December 31, 2012, using the Danish Cardiac Arrest Registry. Patients had a presumed cardiac cause of arrest that was not witnessed by emergency medical services personnel. Data were analyzed from April 1, 2015, to December 10, 2016.

EXPOSURES Nationwide initiatives to facilitate bystander resuscitative efforts, including bystander defibrillation, consisted of resuscitation training of Danish citizens, dissemination of on-site AEDs, foundation of an AED registry linked to emergency medical dispatch centers, and dispatcher-assisted guidance of bystander resuscitation efforts.

MAIN OUTCOMES AND MEASURES The proportion of patients who received bystander defibrillation according to the location of the cardiac arrest and their subsequent 30-day survival.

RESULTS Of the 18 688 patients with OHCAs (67.8% men and 32.2% women; median [interquartile range] age, 72 [62-80] years), 4783 (25.6%) had a cardiac arrest in a public location and 13 905 (74.4%) in a residential location. The number of registered AEDs increased from 141 in 2007 to 7800 in 2012. The distribution of AED location was consistently skewed in favor of public locations. Bystander defibrillation increased in public locations from 3 of 245 (1.2%; 95% CI, 0.4%-3.5%) in 2001 to 78 of 510 (15.3%; 95% CI, 12.4%-18.7%) in 2012 ($P < .001$) but remained unchanged in residential locations from 7 of 542 (1.3%; 95% CI, 0.6%-2.6%) in 2001 to 21 of 1669 (1.3%; 95% CI, 0.8%-1.9%) in 2012 ($P = .17$). Thirty-day survival after bystander defibrillation increased in public locations from 8.3% (95% CI, 1.5%-35.4%) in 2001/2002 to 57.5% (95% CI, 48.6%-66.0%) in 2011/2012 ($P < .001$) in residential locations, from 0.0% (95% CI, 0.0%-19.4%) in 2001/2002 to 25.6% (95% CI, 14.6%-41.1%) in 2011/2012 ($P < .001$).

CONCLUSIONS AND RELEVANCE Initiatives to facilitate bystander defibrillation were associated with a marked increase in bystander defibrillation in public locations, whereas bystander defibrillation remained limited in residential locations. Concomitantly, survival increased after bystander defibrillation in residential and public locations.

Invited Commentary

Supplemental content

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RESEARCH ARTICLE

Home Care Providers to the Rescue: A Novel First-Responder Programme

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Funding: This home care provider first-responder program was funded and organized in a collaboration

Abstract

Aim

To describe the implementation of a novel first-responder programme in which home care providers equipped with automated external defibrillators (AEDs) were dispatched in parallel with existing emergency medical services in the event of a suspected out-of-hospital cardiac arrest (OHCA).

Methods

We evaluated a one-year prospective study that trained home care providers in performing cardiopulmonary resuscitation (CPR) and using an AED in cases of suspected OHCA. Data were collected from cardiac arrest case files, case files from each provider dispatch and a survey among dispatched providers. The study was conducted in a rural district in Denmark.

Results

Home care providers were dispatched to 28 of the 60 OHCAs that occurred in the study period. In ten cases the providers arrived before the ambulance service and subsequently performed CPR. AED analysis was executed in three cases and shock was delivered in one case. For 26 of the 28 cases, the cardiac arrest occurred in a private home. Ninety-five per cent of the providers who had been dispatched to a cardiac arrest reported feeling prepared for managing the initial resuscitation, including use of AED.

The association between driving distance from nearest fire station and survival of out-of-hospital cardiac arrest following early defibrillation by first-responders

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